"COMPARATIVE EVALUATION OF INTRAVENOUS ONDANSETRON (4MG) VERSUS INTRAVENOUS PALONOSETRON (75 MCG) IN THE PREVENTION OF POSTOPERATIVE NAUSEA AND VOMITING IN LAPAROSCOPIC GYNAECOLOGICAL SURGERIES"

Dissertation submitted to

THE TAMILNADU DR. M.G.R.MEDICAL UNIVERSITY

in partial fulfilment for the award of the degree of

DOCTOR OF MEDICINE IN ANAESTHESIOLOGY, BRANCH-X

INSTITUTE OF ANAESTHESIOLOGY & CRITICAL CARE
MADRAS MEDICAL COLLEGE
CHENNAI- 600 003

APRIL 2015

DECLARATION

I solemnly declare that this dissertation entitled **"Comparative Evaluation of Intravenous Ondansetron (4mg) Versus Intravenous Palonosetron (75 mcg) in the Prevention of Postoperative Nausea and Vomiting in Laparoscopic Gynaecological Surgeries"** has been prepared by me, under the guidance of Prof. Dr.G.R Rajashree MD.,DA., Professor of Anaesthesiology, Government Kasturba Gandhi hospital for Women & children, Madras Medical Collage, Chennai in partial fulfillment of regulations for the award of degree of M.D. [Anaesthesiology], examination to be held in April 2015. This study was conducted at Madras Medical Collage, Chennai.I have not submitted this dissertation previously to any university for the award of degree or diploma.

Date:
Place:

Dr.L.Pavithra

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CERTIFICATE

This is to certify that the dissertation titled **"Comparative Evaluation of Intravenous Ondansetron (4mg) Versus Intravenous Palonosetron (75 mcg) in the Prevention of Postoperative Nausea and Vomiting in Laparoscopic Gynaecological Surgeries",** submitted by Dr.L.PAVITHRA in partial fulfilment for the award of the degree of Doctor of Medicine in Anaesthesiology by Tamilnadu Dr.M.G.R. Medical University Chennai is a bonafide record of the work done by her in the Institute of Anaesthesiology and Critical Care, Madras Medical College during the Academic Year 2012-2015.

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“COMPARATIVE EVALUATION OF INTRAVENOUS ONDANSETRON (4MG) VERSUS INTRAVENOUS PALONOSETRON (75 MCG) IN THE PREVENTION OF POSTOPERATIVE NAUSEA AND VOMITING IN LAPAROSCOPIC GYNAECOLOGICAL SURGERIES”

Author Dr.L.Pavithra
Guide: Prof.Dr.G.R.Rajashree, M.D., D.A.,

ABSTRACT

OBJECTIVE

The study was conducted to compare the efficacy of Intravenous Ondansetron (4mg) Versus Intravenous Palonosetron (75 mcg) in the Prevention of Postoperative Nausea and Vomiting in Laparoscopic Gynaecological Surgeries.

METHODOLOGY

100 patients were randomly assigned into two groups of 50 patients. One group of 50 patients received Intravenous Ondansetron (4mg) and the other group of 50 patients received Palonesetron 75mcg intravenously before induction of Anaesthesia.

RESULT

The two groups were found to be similar with respected to Age, Weight, ASA Physical Status, Duration of Surgery and Anaesthesia. There was no significant difference in the incidence of nausea and vomiting between the two groups in the first 0-2hours.

However the incidence of vomiting was significantly reduced in the next 2-48 hours in the Palonesetron group when compared to Ondansetron group. The incidence of drug related adverse effects was not statistically significant.

CONCLUSION

Palonosetron was superior to Ondansetron in the prevention of post operative nausea and vomiting and hence it is safe and reliable to use without any serious adverse effects.

Key Words: Palonosetron, Ondansetron, Post Operative Nausea and Vomiting.

“BIG LITTLE PROBLEM TO THE ANAESTHESIOLOGIST”

INTRODUCTION

Post Operative Nausea and Vomiting is defined as the occurrence of nausea, retching or vomiting during first 24-48 hours after surgery. Post Operative Nausea and Vomiting is the second most common complaint next to pain in the post-operative period.

In the Era of Advanced Medicine and improved Post Operative care, Nausea and Vomiting in postoperative period is a distressing complication which needs attention and prevention.

Of various pathways and triggering factors that have been postulated so far, no exact etiology has been defined.

Numerous factors have been identified in association with Post Operative Nausea and vomiting such as patient age, gender, type of surgery, duration of surgery, anaesthestic factors, smoking, History of motion Sickness, etc.

Among the anaesthesia risk factors inhaled anaesthetics and opiods are the common triggering agents associated with post operative nausea and vomiting.

Post operative nausea and vomiting being an unpleasant experience subjectively, is also associated with very serious adverse complication such as aspiration, wound and suture dehiscence in case of major abdominal surgeries, esophageal rupture, subcutaneous emphysema, pneumothorax.

Post operative nausea and vomiting was found to be the common indication for hospital readmission following day care surgery.

Hence the hunt for an effective antiemetic, thirst for a greater understanding and insight in the prevention and treatment of post operative nausea and vomiting is reflected in the numerous studies that has been conducted so far.

Currently available antiemetic drugs include Dopamine antagonist such as Metoclopramide, Droperidol, haloperidol, H1 receptor antagonist, such as cyclizine, promethazine, anticholinergic such as Atropine and hyoscine, 5HT3 receptor

antagonist such as Ondansetron, Dolasetron, Granisetron, Tropisetron.

Dexamethasone is a proven antiemetic and its mechanism of action is still unknown.

Recently FDA approved aprepitant, a NK-1 receptor antagonist as antiemetic. In the near future, other NK-1 receptor antagonist that is still under trial is expected to enter the market.

Currently 5HT3 receptor Antagonist is considered to be superior to other class of drugs in the prevention of post operative nausea and vomiting but none of the drug is potent enough to completely prevent the incidence of post operative nausea and vomiting. Hence multimodal intervention is advocated in high risk patients susceptible to post operative nausea and vomiting.

5HT3 receptor antagonist is currently used as first-line antiemetic. Among 5HT3 receptor antagonist second generation drug palonosetron was found to be the most effective drug. Very few studies have been carried out to prove the efficacy and potency of this drug.

AIM

The aim of this single blinded interventional prospective study is to compare the effectiveness of intravenous ondansetron (4mg) vs intravenous palonosetron (0.075mg) in the prevention of post operative nausea and vomiting in patients undergoing laparoscopic gynaecological surgery under general anaesthesia.

PHYSIOLOGY OF NAUSEA AND VOMITING

NAUSEA

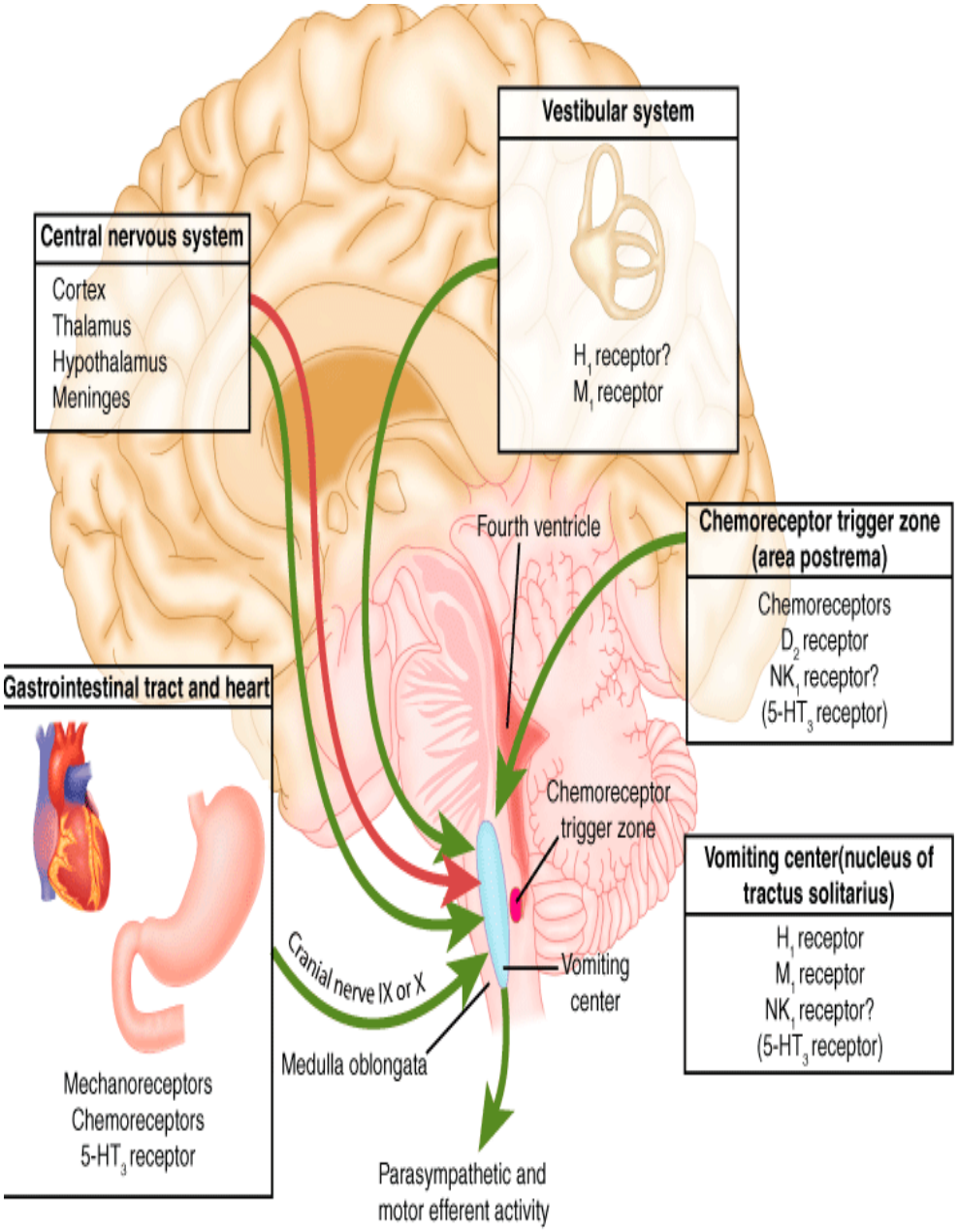
Nausea is defined as an unpleasant sensation with an urge to vomit. It presents with salivation, pallor, sudden cold sweat, followed by reduced gastric tone and contraction of duodenum. It generally precedes vomiting.

RETCHING

It is a strong involuntary effort to vomit and it usually occurs following nausea. The abdominal muscles, diaphgram and chest wall are the muscles actively involved in retching .Expulsion of gastric contents do not occur in retching.

VOMITING

Vomiting is defined as the forceful expulsion of gastric contents through mouth. It is considered to be a defense mechanism to expel the noxious substance present in the intestine. Stomach does not actively take part in vomiting. It is the relaxation of lower esophagel sphincter aided by the active involvement of the diaphgram and the abdominal muscles that facilitates vomiting.


Vestibular system
H1 receptor?
M1 receptor
Central nervous system
Cortex
Thalamus
Hypothalamus
Meninges
Fourth ventricle
Chemoreceptor trigger zone (area postrema)
Chemoreceptors
D2 receptor
NK1 receptor?
(5-HT3 receptor)
Gastrointestinal tract and heart
Chemoreceptor trigger zone
Vomiting center(nucleus of tractus solitarius)
H1 receptor
M1 receptor
NK1 receptor?
(5-HT3 receptor)
Vomiting center
Cranial nerve IX or X
Medulla oblongata
Mechanoreceptors
Chemoreceptors
5-HT3 receptor
Parasympathetic and motor efferent activity

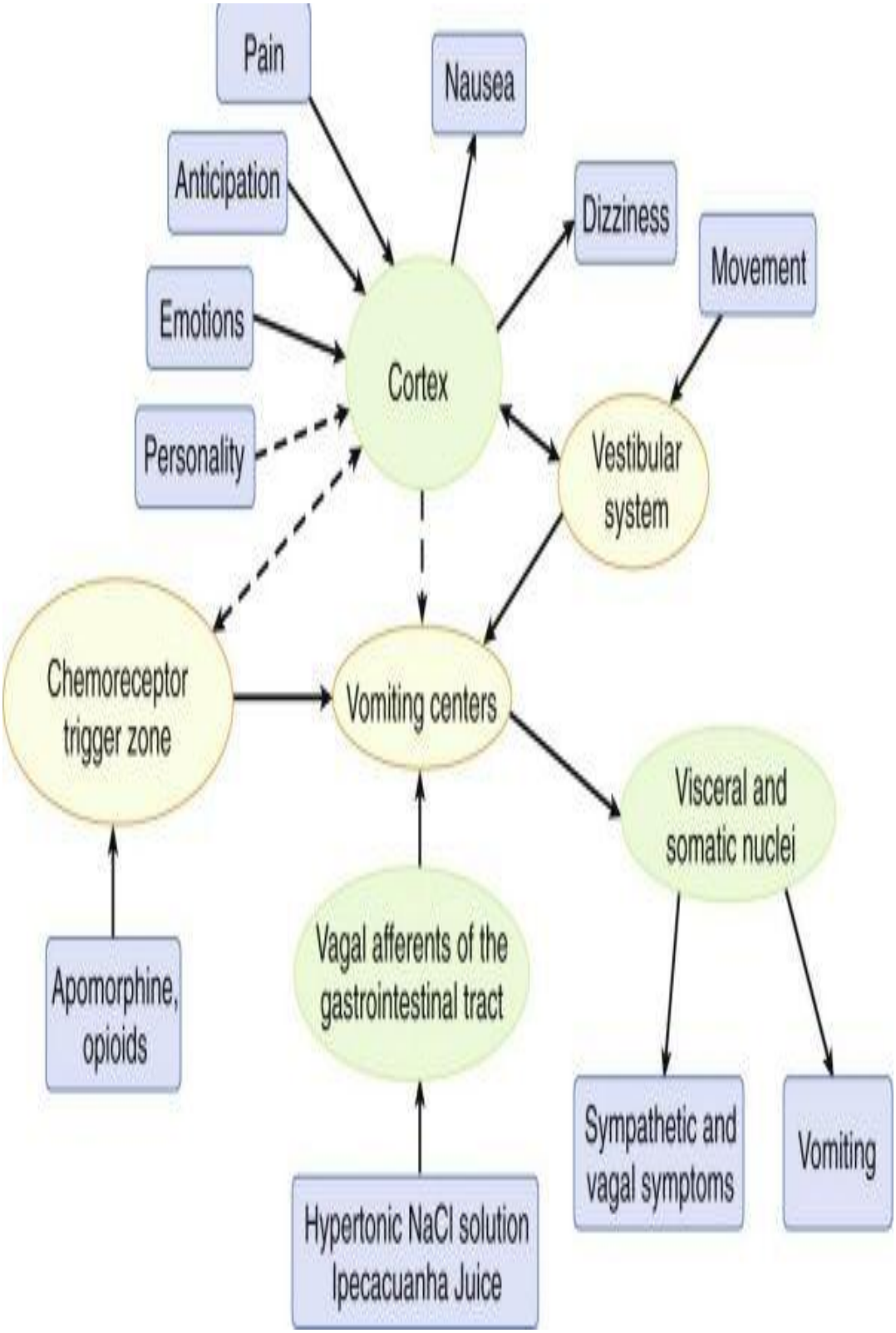
Physiology of post operative nausea and vomiting is complex and it is not completely understood. Recent studies have shown that the brain structures associated with vomiting is present throughout the medulla oblongata and it is not localized to any anatomically defined vomiting center. It includes chemoreceptor trigger zone (CRTZ) located in the area postrema at caudal end of the fourth ventricle and the nucleus tractus solitaries which is present in the area postrema and lower pons.

Chemoreceptor trigger zone is not protected by Blood brain barrier. It receives afferents from the vagus and it can detect toxins and metabolites with emetogenic potential and also the drugs circulating in the blood and cerebrospinal fluid.

Chemoreceptor trigger zone projects neurons to Nucleus Tractus Solitarius which in turn receives vagal afferents and also inputs from limbic and vestibular system.

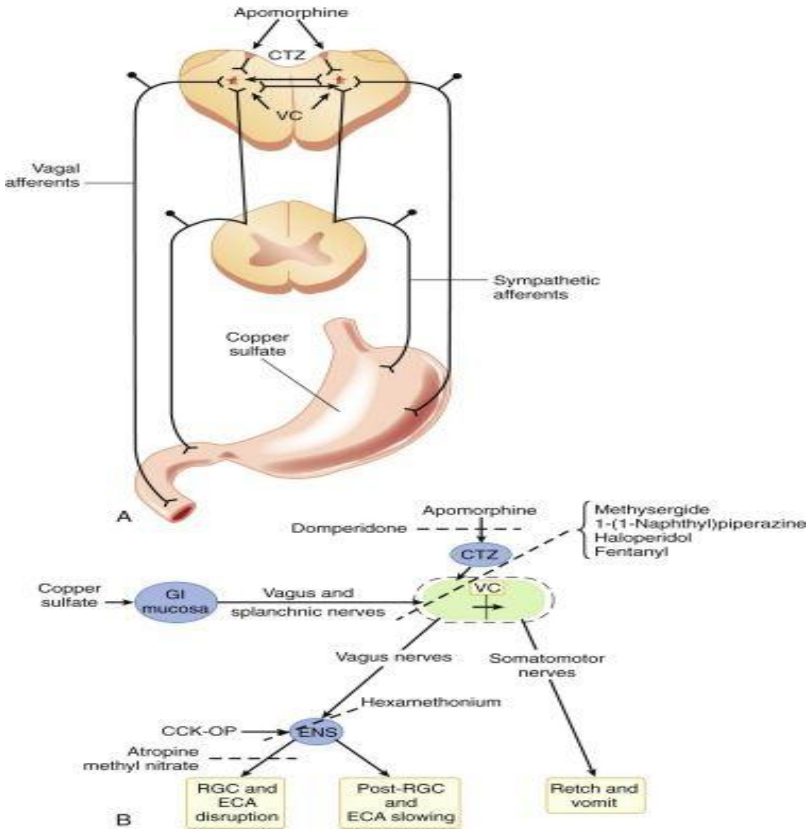
Efferent from Nucleus Tractus Solitarius stimulate the ventral respiratory group and dorsal motor nucleus of vagus, nucleus ambiguous and rostral nucleus to induce vomiting.

Stimulus from the extra medullary center such as limbic system and vestibular system also induces nausea and vomiting as seen in motion sickness, meneire's disease. Psychological stimulus such as anxiety, pain and fear can also induce nausea and vomiting.


Pain
Nausea
Anticipation
Dizziness
Movement
Emotions
Cortex
Personality
Vestibular system
Chemoreceptor trigger zone
Vomiting centers
Visceral and somatic nuclei
Apomorphine, opioids
Vagal afferents of the gastrointestinal tract
Sympathetic and vagal symptoms
Vomiting
Hypertonic NaCl solution Ipecacuanha Juice

PATHWAY OF NAUSEA AND VOMITING

Toxic substance in the gut stimulates the release of 5HT from enterochromaffin cell which constitutes 90% reserve of the total 5-HT in our body. 5-HT is released in close proximity to the vagal afferent. Nucleus Tractus Solitarius receiving afferent from vagus induces vomiting. Vagal afferents are of two types.



Mechanoreceptors in the muscular layer is activated by contraction and distension of the muscular wall of the gut. Chemoreceptor in the lumen of the gut responds to noxious substance in the gut.

Absorbed toxin and drugs stimulate CRTZ, a circumventricular organ which lacks Blood brain barrier, which in turn triggers Nucleus Tractus Solitarius in the Brainstem to induce vomiting.

Numerous receptors are identified in the CRTZ. But it is still unclear why the agonist can't induce vomiting whereas the antagonist is effective in preventing vomiting.

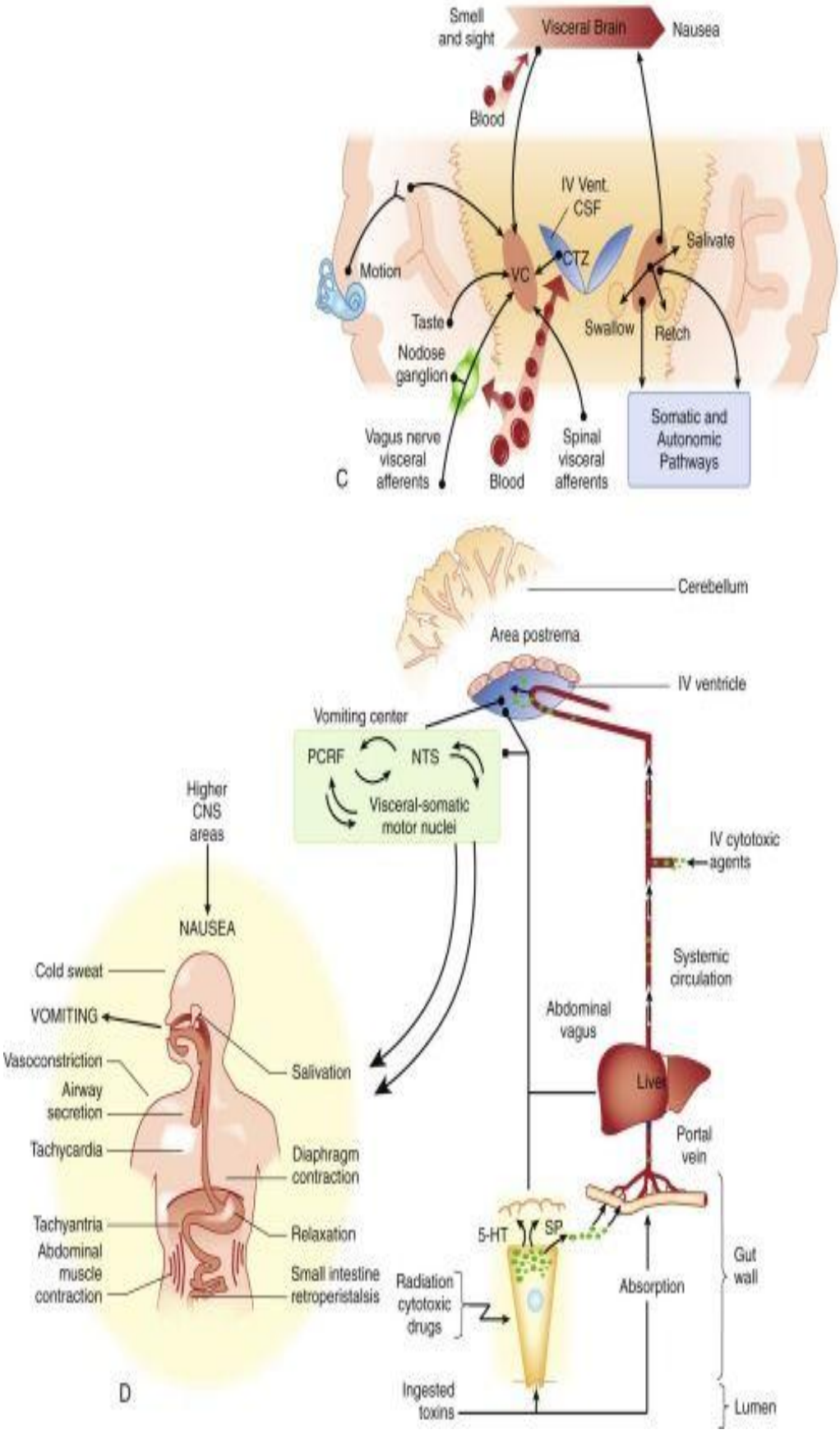
Serotonin is also released by stimulation of M3 receptors, Beta adrenoceptors and H3receptors. The stimulation of GABA B receptors, 5-HT4 receptor and Alpha 2 adrenoceptor and Vasoactive Intestinal Polypeptide & Somatostatin was found to reduce the release of serotonin.

Post Operative Nausea and Vomiting after major abdominal surgery is attributed to the release of serotonin which is evident by the presence of metabolite, 5-Hydroxy acetic acid in the urine.

Stimulation of vestibular system results in emesis as seen in motion sickness, meniere’s disease.

Head injury, infection of the meninges and brain, space occupying lesion in the brain which usully presents with increased intracranial pressure usually presents with nausea and vomiting.

Acute metabolic changes such as high blood sugar and rampant hormonal changes that occurs in pregnancy also induces nausea and vomiting.


Smell and sight
Visceral Brain
Nausea
Blood
IV Vent. CSF
CTZ
VC
Salivate
Motion
Taste
Swallow
Retch
Nodose ganglion
Vagus nerve visceral afferents
Blood
Spinal visceral afferents
Somatic and Autonomic Pathways
C
Cerebellum
Area postrema
IV ventricle
Vomiting center
PCRF
NTS
Visceral-somatic motor nuclei
Higher CNS areas
IV cytotoxic agents
NAUSEA
Systemic circulation
Cold sweat
VOMITING
Abdominal vagus
Vasoconstriction
Salivation
Airway secretion
Liver
Tachycardia
Portal vein
Diaphragm contraction
Tachyantria
Relaxation
5-HT
SP
Abdominal muscle contraction
Small intestine retroperistalsis
Radiation cytotoxic drugs
Absorption
Gut wall
Ingested toxins
Lumen
D

FACTORS ASSOCIATED WTH POST OPERATIVE NAUSEA AND VOMITING

PATIENT RELATED FACTORS:-

Gender

Female gender is an independent risk factor for Post Operative Nausea and Vomiting. Incidence of Post Operative Nausea and Vomiting is two to three times higher in woman than in men.

Age

Incidence of post-operative nausea and vomiting increases with age. It is least in infants , increases until late childhood and remains constant in adults.

Body Habitus

Incidence of post-operative nausea and vomiting is greater in obese than in asthenic patients.

Smoking

Non-smokers were 1.8 times more likely than smokers to have post-operative nausea and vomiting. Nicotine stimulates indirect GABA mediated cerebral dopamine

release. Reduced incidence of post-operative nausea and vomiting in smokers is attributed to the withdrawal of nicotine in the perioperative period which results in low dopamine levels.

History of post-operative nausea and vomiting, motion sickness and migraine are independent predictors of post-operative nausea and vomiting.

ANAESTHESIA RELATED FACTORS:

Regional Vs General Anaesthesia

General Anaesthesia is associated with high incidence of nausea and vomiting when compared with Regional Anesthesia.

General Anaesthesia is attributed to the high incidence of post-operative nausea and vomiting probably due to use of numerous drugs and anaesthetic gases. Among the induction agents, propofol is associated with lower incidence of post-operative nausea and vomiting and it has antiemetic property at low does.Use of Ketamine is significantly associated with nausea and vomiting in the post operative period.

Nitrous oxide is also an highly emetogenic gas which when used in combination with volatile anesthetic is found to have additive emetogenic effect.

All the volatile anaesthetics that are currently in use are emetogenic and severity of individual volatile anaesthetic has not been elucidated so far.

Opioids

The superior quality of analgesia obtained from the opioids makes it the most needed drug of choice for Anaesthesiologist who are dealing with pain management. One of the most common side effect of opioids is nausea and vomiting

Increased usage of opioids such as morphine and fentanyl for analgesia is associated with nausea and vomiting in the post-operative period.

Meta analysis of various studies shows that irrespective of the type of opioid, the dose of opioids is an important determinant factor for post-operative nausea and vomiting.

Duration of Anaesthesia is also an independent risk factor for post-operative nausea and vomiting. Longer

duration of surgery implies longer duration of anesthesia and the use of volatile agents itself is an independent risk factor for post-operative nausea and vomiting.The incidence of post-operative nausea and vomiting is high in invasive procedures.

Bag and mask ventilation results in gastric distension and induces emesis due to entrapment of air in the stomach.

Airway manipulation during laryngoscopy ,intubation and extubation will result in mechanoreceptor stimulation via vagus and glossopharyngeal nerve resulting in emesis.

Neuromuscular reversal using neostigmine, an anticholinesterase inhibitor is associated with post-operative nausea and vomiting.

Sudden and rapid movement of head and neck while shifting the patient can induce nausea and vomiting.

SURGERY RELATED FACTORS

The incidence of post-operative nausea and vomiting depends on the type of surgery as well. Middle ear surgeries, ENT surgeries such as adenotonsillectomy and surgery involving the larynx which are frequently associated with swallowing of blood is associated with high incidence of post-operative nausea and vomiting.

Major abdominal surgery which are associated with large release of serotonin from the gut, peritoneal irritation in laparoscopic surgery and vagal stimulation in gynaecological procedures are also attributed to the incidence of nausea and vomiting in post operative period following these surgeries.

Middle ear surgeries such as Tympanoplasty done under general anaesthesia results in diffusion of nitrous oxide and rise in the middle ear pressure .This results in the stimulation of vestibular afferents which results in vomiting. Arnold's nerve, auricular branch of vagus nerve which supplies the tympanum also induces emesis when stimulated.

PERIOPERATIVE FACTORS

Anxiety and stress increases the risk of post-operative nausea and vomiting which is mainly due to release of adrenaline and gastric distension as a result of swallowing of air.

In patient with delayed gastric motility, such as diabetes mellitus and pyloric stenosis, risk of post-operative nausea and vomiting is high.

Induction of anaesthesia shortly after the intake of food is found to be associated with post-operative nausea and vomiting. This is attributed to the increased release of serotonin in the hepatic circulation following a meal.

Since Post-operative nausea and vomiting is attributed to multiple risk factors, predictive risk score have been defined based on meta analysis of various studies

Koivuranta et al . , proposed a simplified risk score for children. The parameters in the risk stratification includes female gender, non smoking status, history of post-operative nausea and vomiting, history of motion sickness and duration of surgery >60min. If 0,1,2,3,4 or 5 risk factors are present,

the risk of incidence of post-operative nausea and vomiting is 17%, 18%, 42%, 54%, 74% and 87% respectively.

Apfel et al ., defined a simplified risk scoring system for adult. Apfel's risk score consist of 4 factors instead of 5 in koivuranta et al. Apfel's risk score includes female gender, history of post-operative nausea and vomiting, motion sickness, non smoking status and post-operative use of opiods. If 0,1,2,3 & 4 factors are present, the risk of nausea and vomiting in post-operative is 10%, 20%, 40%, 60%or 80% respectively.

POVOC score is another simplified risk score for predicting post-operative nausea and vomiting is children, it includes duration of surgery ≥30 min, age ≥ 3 years, strabismus surgery and history of post-operative vomiting in the child / relatives. If 0,1,2,3 and 4, risk factors are present the incidence of post-operative nausea and vomiting is 9%,10%,30% 55% and 70% respectively.

Antiemetic prophylaxis differs from patient to patient based on the presence of risk factors.

Hence the risk of nausea and vomiting in post operative can be best predicted by simplified score rather than assessing the numerous risk factors.

This implies to the post operative nausea and vomiting prophylaxis strategy as well. It should be tailored based on the patient risk factors. Such high risk patient gets absolute risk reduction from effective intervention.

ANTIEMETICS

Currently used antiemetics in the prevention and management of Post Operative Nausea and Vomiting includes Dopamine antagonist such as metoclopramide, Droperidol, Haloperidol, Alizapride, Perphenazine, and prochlorperazine, H1 receptor antagonist such as Dimenhydrinate, cyclizine, and promethazine, anticholinergics include hyoscine, atropine, serotonin receptor antagonist namely ondansetron, dolasetron, granisetron, tropisetron and GABA receptor agonist diazepam, lorazepam and Midazolam.Recently, neurokinin 1 receptor antagonist aprepitant is added to the class of antiemetics. Dexamethasone is also used in the prevention of nausea and vomiting. The mechanism of action is still not known.

DOPAMINE ANTAGONIST

Dopamine antagonist exerts its antiemetic effect via D2 receptor. Metoclopramide was initially used in the treatment of chemotherapy induced nausea and vomiting. Based on clinical studies, 10mg was found to be effective in the prevention of Post Operative Nausea and Vomiting. Large doses is associated with side effects such as hypotension, tachycardia and other notable side effects such as dyskinesia and extrapyramidal symptoms.

Droperidol, a potent D2 antagonist has antiemetic effect in the dose range of 0.625-1.25mg. Even with minimal dose, side effects such as anxiety, akasthisia, dystonia and restlessness can occur. Droperidol is contraindicated in patients with long Q-T interval. FDA gave black box warning to haloperidol in view of arrythmias in patients with long QT syndrome.

Other Dopamine antagonist such as Alizapride, Prochlorperazine and perphenazine are not routinely used.

HISTAMINE ANTAGONIST

H1 receptor antagonist, Diphenhydramine and Dimenhydrinate which are used in the treatment of motion sickness posses anticholinergic activity as well. All H1 antagonist have sedation as the most common side effect. other Side effects include headache, urinary retention dry mouth, blurred vision and drowsiness. vascular necrosis, a very rare and infrequent complication have also been documented.

ANTICHOLINERGICS

Atropine was found to be more effective in preventing nausea and vomiting than glycopyrolate. It is useful in motion induced nausea and vomiting as well. Scopolamine, a short acting anticholinergic which is also an effective antiemetic is associated with increased incidence of side effects such as dry mouth, agitation, blurring of vision and dizziness.

DEXAMETHASONE

Dexamethasone exerts its pharmacological antiemetic effect through central inhibition of nucleus tractus solitarius. It has a slow onset of action and its efficacy is similar to

ondansetron. It is effective in very low dose of 2-5mg intravenously.

NEUROKININ ANTAGONIST

Neurokinin 1 receptors are found in the vagal afferents in the gut. substance P, a regulatory polypeptide induces emesis via neurokinin receptors present in vagus. Aprepitant, NK 1 receptor antagonist is currently in use as an antiemetic. Other drugs of this class, Casopitant and Rolapitant is expected to enter the market shortly.

OTHER ADJUVANT THERAPIES

Ginger is assumed to have antiemetic property but studies have not proved any definite mechanism of action. Infusion of liberal crystalloids and adequate hydration was found to reduce the incidence of nausea.

5HT3 RECEPTOR ANTAGONIST AND POST OPERATIVE NAUSEA AND VOMITING

5-HT3 receptor antagonist is considered to be superior among the available class of antiemetics.Serotonin receptor antagonist drugs are highly selective drugs that acts only on 5HT3 receptors sparing other cholinergic, histamine and dopamine receptors. When compared to the other available antiemetics , this group of drug is found to be more potent with minimal sideeffects. 5-HT3 receptors are present in vagal afferents, the nucleus tractus solitarius and the area postrema. Eventhough all 5-HT3 receptor antagonist have same mechanism of action they have difference in affinity at the receptor level due to the difference in the chemical structure.All the drugs in this group are metabolized by cytochrome P450 in different path ways.

Ondansetron, a carbazole derivative is a strong antagonist of 5-HT3 receptor with weak 5-HT4 antagonistic activity.It has a half life of 3.9 hours and it is metabolized by CYP1A1/2,CYP2D6,CYP3A3/4/5. The drug is administered at a dose of 0.15mg per Kg.

Granisetron is a indazole derivative with 5-HT3 receptor antagonistic activity.It undergoes metabolism by CYP3A3/4/5 and it has a half life of 9-11 hours.The dosage of the drug is 10 microgram per Kg.

Dolasetron, a indole derivative with a half life of 7-9 hours is a selective 5-HT3 receptor antagonist. It undergoes metabolism similar to Granisetron and also by CYP2D6. It is administered at a dose of 0.6 – 3 mg per Kg.

Palonosetron, an isoquinoline derivative drug has highest affinity for 5-HT3 receptor among all 5-HT3 receptor antagonist. The unusual and prolonged half life of around 40 hours makes this drug distinct among 5-HT3 receptor antagonist.Palonosetron is metabolized by Cytochrome P450 (CYP1A2, CYP2D6, CYP3A3/4/5). This drug was commonly used in the prevention of chemotherapy indused nausea and vomiting at a dose of 0.25mg single intravenous bolus.

Ramosetron with selective action only at 5-HT3 receptor is a benzimidazole derivative, with a half life of around 6 hours.The metabolic pathway has not been clearely

elucidated so far.It is administered at a dose of 300 micogram per Kg.

Tropisetron is an indole derivative with selective action only at 5-HT3 receptor and it is used in the dose of 200 microgram per Kg. It is metabolized by CYP3A3/4/5, CYP2D6 with a half life of 5.6 hours.

Serotonin receptor antagonist have been associated with very few side effects such as headache, constipation and dizziness. It does not produce unwanted side effects like sedation and extrapyramidal symptoms which is seen with antihistamine drugs.

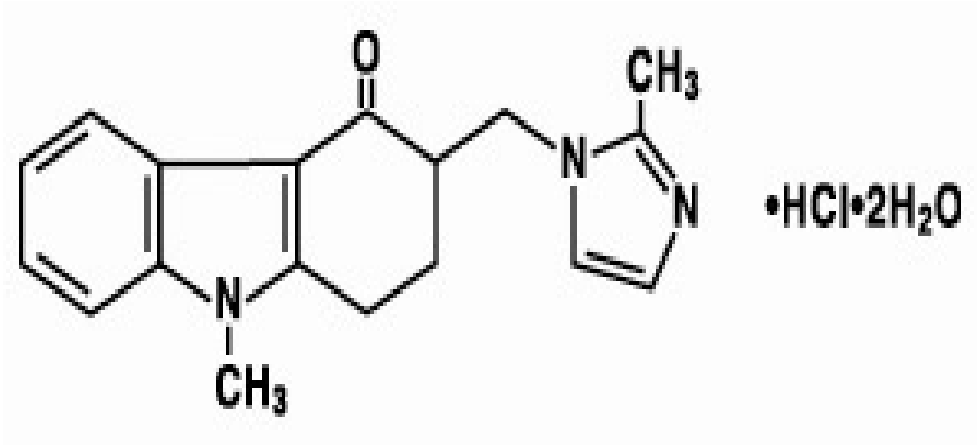
A very rare and infrequent adverse effect of serotonin receptor antagonist is the incidence of cardiovascular rythym abnormalities like prolongation of PT and QT interval in electrocardiogram.

Serotonin receptor antagonist is used in the management of chemotherapy induced nausea and vomiting and post operative nausea and vomiting.It is not effective in motion sickness.

5-HT3 receptor antagonist is currently preferred as the first line of antiemetic in the management of post operative nausea and vomiting due to its high receptor selectivity and minimal side effects.

PHARMACOLOGY OF ONDANSETRON

Ondansetron is a selective 5-HT3 receptor antagonist.It is chemically 1, 2, 3, 9 tetrahydro 9-methyl-3-[(2-methyl-1 H imidazole-1-ylmethyl-4H-Carbazol-4-one monohydrochloride dihydrate (C18 H19 N3O. Hcl-2H20). It's estimated molecular weight is 365.9.



PHYSICAL PROPERTIES

Ondansetron hydrochloride is a white to off-white powder obtained by chemical synthesis. It is soluble in water (3.2/W/W) and in 0.9% Sodium chloride (0.8% W/V). The drug dosage is expressed in milligram.

PHARMACODYNAMICS

Serotonin receptors are distributed both centrally and peripherally. ondansetron is primarily a 5HT3 receptor antagonist. Ondansetron's antiemetic action is still unclear whether it is mediated via central receptor or peripheral receptors or both .It has no effect on gut motility, small intestine transit time or its sphincter tone. Interaction of ondansetron with general and local anesthetics is not known.

Ondansetron does not have any effect on respiratory depressant effect induced by narcotics.

It does not have interaction with any muscle relaxants and does not alter the degree of neuromuscular blockade produced by non-depolarising relaxants.

PHARMACOKINETICS

It is administered by Oral / Parentral (intravenous / intramuscular) route. It is completely absorbed from the gastro intestinal tract after oral uptake and it does not accumulate with repeated administration. Intake of drug after a meal is found to increase the bioavailability. The plasma concentration of the drug reaches peak concentration after 0.5

to 2 hours since the time of intake. Due to first pass metabolism in liver, bio-available of the drug is only about 60%.Other routes of administration include intramuscular, subcutaneous and rectal administration.

Plasma half life of ondansetron is 3-4 hours and the rate of clearance is 541ml/min and it is reduced with increasing age and hepatic impairment. Dosage needs to be reduced in old age because of increased bioavailability due to reduced first-pass hepatic metabolism and a prolonged half life of 4-5 hours.

Volume of distribution of drug is approximately around 160L and it moderately binds to plasma proteins (70 to 76%).Pediatric age groups and patients with hepatic disease have large volume of distribution.

It crosses the blood-brain barrier and concentration of the drug in cerebrospinal fluid measures about 10% of the plasma concentration.

95% of the drug undergoes metabolism in the liver and the remaining 5% is excreted unchanged in urine. The primary pathway involved in the metabolism of ondansetron

is initially indole ring hydroxylation which then undergoes glucoronide or sulfate conjugation. The enzyme involved in metabolism is cytochrome P-450 (CYP3A4, CUP2D6, CYPIA2).

Hence drugs that induces or inhibits the enzymes cytochrome P450 has significant effect on the metabolism of the drugs and its duration of action.

Phenytoin, rifampicin and carbamazepine induces the enzyme CYP3A4 and it significantly increases the clearance of the drug which reduces the plasma concentration and hence the half life of drug.

The metabolic end products are conjugates of 7-hydroxy and 8-hydroxy ondansetron. The end products are not metabolically active and they are excreted via kidneys.

PREPARATION

Oral - 4 or 8 mg of ondansetron Hcl. Dihydrate.

PARENTERAL FORMULATION

It is available as aqueous solution containing 2mg/ml of ondansetron hydrochloride dihydrate, sodium chloride 9.0mg USP, citric and monohydrate 0.5mg USP, and 0.25mg of of

sodium citrate dihydate USP, the shelf-life of the drug is 8 years. It is compatible with 0.9% Normal Saline, Ringer Lactate and 5% dextrose containing solution.

It is administered i.v over a period of 2-5 minutes.

THERAPEUTIC USAGE

Ondansetron is primarily an antiemetic used in the treatment of post-operative nausea and vomiting. It is the preferred antiemetic in patients undergoing highly emetogenic radiotherapy and chemotherapy with drugs such as high dose cisplatin.

It is contraindicated in patients with known hypersensitivity to ondansetron. Hypersentive reaction have been reported in patients who are hypersensitive to other class of 5HT3 receptor antagonist.

DOSAGE

CHEMOTHERAPY INDUCED NAUSEA AND VOMITING(CINV)

The recommended intravenous dosage of drugs for adults is single dose of 32mg iv or 0.15mg/kg. Single dose of

32mg is administered intravenously before the initiation of chemotherapy over a period of 15 minutes. In three dose regimen Subsequent doses (0.15mg/kg) are administered at 4th and 8th hour after the first dose.

In paediatric age group, three doses of 0.15mg/kg is given. After the initial dose of 0.15 mg/kg which is given half an hour before the initiation of chemotherapy, subsequent doses are given 4 and 8 hours apart.

POST-OPERATIVE NAUSEA AND VOMITING

The adult dosage for post-operative nausea and vomiting is 4mg ondansetron administered slow i.v. over 2-5 minutes before induction. 4mg is the fixed dose for patients weighing more than 40 kg.

The recommended dosage of ondansetron is 0.1mg/kg for children weighing less than 40kg infused over a period of 2-5 minutes.

Geriatric dose is same as that recommended for adult patients.

ADVERSE REACTION

Headache, diarrhea, fever, akasthisia, Acute dystonic reactions are reported in patients receiving ondansetron at a dose of 0.15mg/kg.

CNS:

Symptom similar to extrapyramidal reaction have been reported. Rarely Grand-mal seizures can occur.

CARDIO-VASCULAR

Chest Pain, Angina, ECG Changes, Tachycardia, Hypotension can occur.

GASTRO INTESTINAL

Constipation was reported in patients receiving ondansetron for Chemotherapy induced nausea and vomiting.

HEPATIC

Transient elevation of liver enzyme about two to three times normal is seen in patient with normal Liver function test who have undergone chemotherapy.

LOCAL REACTION

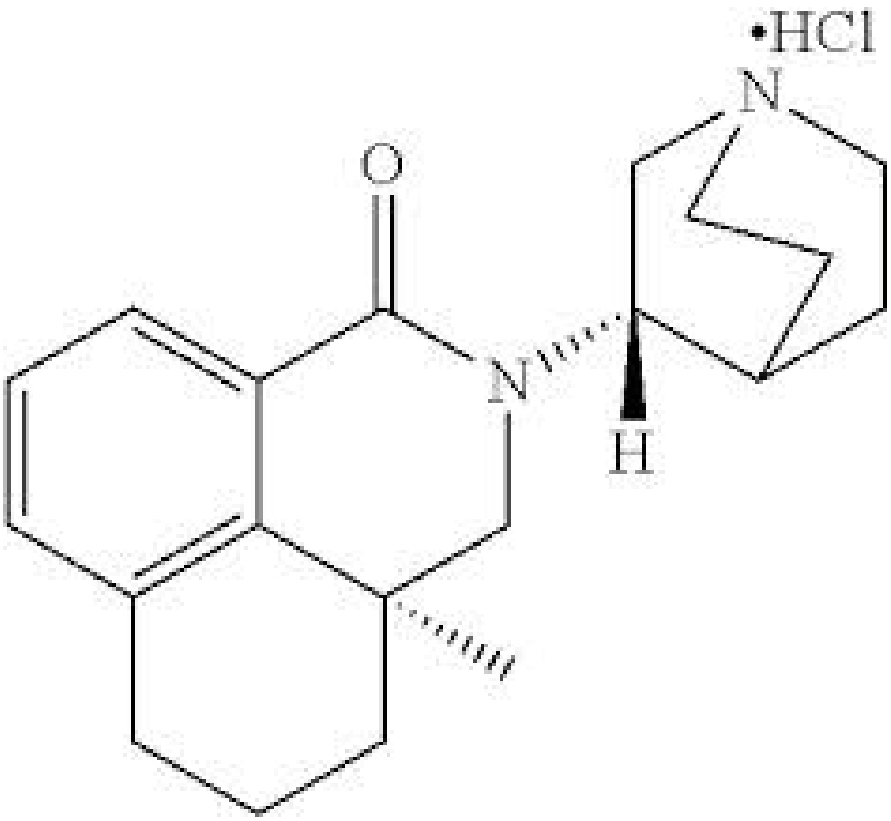
Pain, redness, itching, and rash can occur at the site of inection.

Other rare adverse effects include dizziness, musculo skeletal pain, sedation, swelling anxiety, pruritus, paresthesia, urinary retention and dysuria.

PHARMACOLOGY OF PALONOSETRON

PALONOSETRON HYDROCHLORIDE

Palonosetron is a second generation selective 5HT3 receptor antagonist. palonosetron hydrochloride is chemically (3aS) -2-(CS)-1-Azabicyclo (2,2,2) Oct-3-yl) – 2,3,3a,4,5,6 – hexahydro-1-0x01Hbenz[de] isoquinolone hydrochloride. The molecular formula is expressed as C19H24N2O.Hcl.It has a estimated molecular weight of 332.87. The structural formula for palonosetron is



It has no isomers and it exist as a single structure .

PHYSICAL PROPERTIES

It is a white crystalline powder. It is readily soluble in water and it does not exhibit isomerism inspite of two chiral centres.

It is synthesized chemically in a five step process. It is a clear, sterile, colorless, buffered isotonic solution and it is non-pyrogenic. It is available in 5ml vial in the concentration of 0.25 mg palonosetron hydrochloride per ml of drug with other constituent such as 207.5 mg mannitol, citrate buffer, disodium edetate for intravenous administration. The pH varies between 4.5 to 5.5

It is also available in 1.5ml vial with base drug of 0.075 mg palonosetron containing 0.084mg palonosetron hydrochloride, 83 mg mannitol, citrate buffer and disodium edetate in water for intravenous administration.

Shelf-life of the intravenous formulation of the drug is round 1-2 years.

MECHANISM OF ACTION

Palonosetron is believed to be the most-effective 5HT3 receptor antagonist due to its unique property of allosteric binding to 5HT3 receptors with the subsequent receptor internalization and negative co-operativity with neurokinin 1 receptor. Palonosetron has a long half life of 40 hour with 30 times higher receptor affinity than first generation. It has a very long half life of 40 hours. It binds to 5HT3 receptors located in the nerve terminals of vagus in the periphery and chemoreceptor trigger zone in the area postrema.

PHARMACOKINETICS

After intravenous administration of palonosetron, there is a initial decline in the plasma concentration of the drug followed by slow elimination from the body. The volume of distribution of palonosetron is approximately 6.9 to 7.9 l/kg. 62% of the drug is bound to plasma proteins.

50% of palonosetron is metabolized primarily via hydroxylation to form two primary metabolites namely N-oxide palonosetron and 6-8 hydroxy-palonosetron. Around 1% of the primary metabolites of palonosetron have residual

antagonistic effects. palonosteron is primarily metabolized by CYP2D6 and also to a lesser extent by CYP3A4 and CYP1A2.

The metabolic end products are eliminated via renal excretion. Total body clearance of palonosetron is 160 + 35 ml/h/kg and the renal clearance of the drug was around 66.5 $\pm$ 18.2 ml/h/kg. The mean elimination half life of the drug is 40 hours which is due to the low total body clearance and large volume of distribution of drug . Terminal elimination half life may extend beyond 100 hrs

Age and gender do not affect the pharmacokinetics of palanoseteron. In patients with mild to moderate renal impairment pharmacokinetics of the drug is not much altered. severe renal impairment alters the pharmacokinetics and reduces renal clearance. Dose reduction is required in patients with severe hepatic impairment.

THERAPEUTIC INDICATION

Palonosetron is used in the prevention of nausea and vomiting following highly emetogenic chemotherapy.

It is used in the treatment as well as prophylaxis of post-operative nausea and vomiting.

Contraindicated in patients with known hypersensitivity to the drug and also to other class of 5HT3 receptor antagonist.

DRUG INTERACTIONS

Study receptor knows that palonosetron is not an inhibitor of CYP1A2, CYP2A6, CYP2B6, CYP2C9, CYP2D6, CYP2E1 and CYP3A4/5. Neither it induces the activity of CYP1A2, CYP2D6 or CYP3A4/5.

Palonosetron does not interact with any chemotherapeutic drugs nor interfere with the anti-tumor activity of the drug.

Palonosetron does not have any significant interaction with metoclopramide which is a CYP2D6 inhibitor.

SAFETY PROFILE

Animal studies have shown no effect on fetal development at low doses. At high doses, fetal weight

reduction was observed. Hence it is not advisable during pregnancy.

Palonosteron is not advised during lactation since it is not known wether the drug is excreted in Breast milk.

DOSAGE

CHEMOTHERAPY INDUCED NAUSEA AND VOMITING (CINV):

The recommended dose is 250mg administered as a single dose 30 minutes before the initiation of chemotherapy.

POST OPERATIVE NAUSEA AND VOMITING

Single dosage of 0.075 mg palonosetron is administered intravenously over a period of 10 seconds before induction of anaesthesia

ADVERSE REACTION

Cardiovascular

Hypotension and tachycardia can occur.Very rare complications include hypertension, angina, rhythm abnormalities, supraventricular extrasystoles and

prolongations of QT interval. The incidence of these complication is less than 1%.

CENTRAL NERVOUS SYSTEM

Headache, dizziness, paresthesia, insomnia, somnolence, anxiety.

HEPATIC

Transient elevation of liver enzymes such as AST & ALT can occur in patients receiving chemotherapy.

GASTROINTESTINAL

Constipation, dyspepsia, abdominal pain, dry mouth and flatulence.

METABOLIC

Hyper/hypokalemia, anorexia and hyperglycemia.

DERMATOLOGIC

Allergic dermatitis, rash and irritation at the site of injection.

OTHERS

Very rare complication include urinary retention, glycosuria, Arthralgia, Hyperbilirubinemia, tinnitus, eye irritation.

REVIEW OF LITERATURE

Yu Yil Kim et al., compared palonosetron with ondansetron in the prevention of post-operative nausea and vomiting in patients receiving intravenous patient controlled analgesia.This randomized interventional study was done in patients undergoing laparoscopic gynaecological surgery. Patients involved in study group were assigned randomly into two equal groups. One group received intravenous ondansetron 8mg iv bolus and 16 mg added to IV-PCA mixure. Another group received palonosetron 75 mcg i.v single bolus dose. The incidence of nausea, vomiting and side effects were recorded at 2,24,48,& 72 hour post operatively. The results from the study showed that there was no difference in the incidence of Post Operative Nausea and Vomiting during 72 hr period. The incidence of vomiting in ondansetron group was 18% compared to 4% in palonosetron group.It was observed that palonosetron was be superior to ondansetron in the preventing the incidence of post operative nausea and vomiting.

Moon Ye et al., compared the antiemetic effect of ondansetron and palonosetron in patients who underwent thyroidectomy and received opioid based PCA. In this prospective, randomized double blind study, consisting of 100 patients, two groups consisting of 50 patients were randomly assigned to receive palonosetron 0.075 mg and ondansetron 8mg intravenous bolus followed by the addition of 16mg to PCA mixture containing fentanyl. Episodes of nausea, vomiting, severity of nausea, requirement of rescue antiemetic and adverse effects were observed over a period of 24 hours. There was no significant difference between two group during the first 2 hours. But, during 2-24 hr, incidence of nausea and vomiting was lower in the palonosetron group than in the ondansetron group. The incidence of Post Operative Nausea and Vomiting in palonosetron group was 42% when compared to 62% in the ondansetron group. Palonosetron was found to be more effective than ondansetron in the prevention of Post Operative Nausea and Vomiting 2-24 hr after surgery.

Park SK, Cho EJ evaluated the efficacy of palonosetron and ondansetron in the prevention of Post Operative Nausea and Vomiting in female patients undergoing gynaecological laparoscopic surgeries. In a randomized double blind trial consisting of 90 patients, two groups of 45 patients each were randomnly assigned to receive ondansetron 8mg intravenously and palonosetron 0.075 mg intravenously before induction of anaesthesia. The occurrence of nausea and vomiting and severity of nausea was studied for a period of 24 hours. The incidence of Post Operative Nausea and Vomiting was 42.2% in the palonosetron group compared to 66.7% in the ondansetron group. Palonosetron 0.075 mg was found to be more superior and efficacious than ondansetron in preventing Post Operative Nausea and Vomiting.

Bajwa SS et al., in a prospective double blind study compared the antiemetic effect of ondansetron and palonosetron. Study was carried out in patients undergoing laparoscopic gynaecological surgery and subjects were randomnly assigned into two groups to receive intravenous palonosetron 75mcg and ondanseteron 8 mg intravenously.

The incidence of nausea was 20% in the ondansetron group when compared to 6.67% in the palonosetron group. The incidence of vomiting was 13.3% in the ondansetron group compared to 3.3% in the palonosetron group. There was no significant difference in the incidence of adverse effect between the two groups. Palonosetron was found to be superior and effective in the prevention of post operative nausea and vomiting when compared to ondansetron.

Candiotti et al., conducted a placebo controlled study in a group of 574 patients who underwent gynaecological laparoscopic surgery to assess the efficacy and safety profile of three different doses of palonosetron. patients were stratified based on the risk factor and patients with $\geq$ 2 risk factors were assigned to receive one of the three doses of intravenous palonosteron (0.025 mg, 0.050 mg or 0.075 mg) before induction of anaesthesia. Complete response to the drug was observed over a period of 72 hours in the post-operative period. Compared to placebo group, patients who received palonosetron were associated with less incidence of Post Operative Nausea and Vomiting. Complete response is defined when there is no

emetic episodes and no requirement of resue antiemetic. Complete response in placebo group was 26% when compared with 43% in palonosetron group in the first 0-24 hours whereas it was 41% in placebo and 49% in palonosetron group in 24-72 hours. The incidence and severity of nausea was comparatively low in the palonosetron group when compared to placebo group. Of the three doses, single dose of Palonosetron 0.075 mg was found to be effective in preventing the incidence of nausea and vomiting.

Rojas C et al., described the unique mechanism of interaction of palonosetron at the receptor level. They conducted experiments on receptor site saturation binding to examine competitive versus potential allosteric binding between Ondansetron, Palonosetron, Granisetron & 5HT3 receptor. on the basis of the experiment, it was found that palonosetron has unique mechanism of allosteric binding at the receptor level that differentiates it from other 5-HT3 receptor antagonist..

Shadangi BK et al., did a randomize double blind study to compare the efficacy of intravenous ondansetron

and palonoestron in the prevention of post-operative nausea and vomiting. 90 patients undergoing general anaesthesia were divided into three groups containing 30 members each. one group received placebo injection, the second group received ondansetron 8 mg iv and the third group received palonosetron 0.075 mg before induction of anaesthesia. Patients were followed up on this post-op period for the incidence of nausea and vomiting at 1,2,6,12 and 24 hours. It was observed that there was no significant difference between Ondansetron and Palonosetron in the incidence of vomiting but the incidence of nausea was significantly less in the palonosetron group than ondansetron group which was significantly less than palcebo group. Palonosetron was found to be more effective and superior than ondansetron in the prevention of Post Operative Nausea and Vomiting.

Blitz JD et al., evaluated the efficacy of palonosetron with dexamethasone combination versus palonosetron alone in a randomized double blind study. The study group consist of 118 patients scheduled to

undergo laparoscopic surgeries.patients with more than three risk factors were included in the study.subjects were randomized into two groups of 59 each to receive a combination of 8 mg of dexamethasone plus 0.075mg of palonosetron and the other group received equivalent volume of saline plus 0.075mg of palonosetron. Patients were followed up for a period of 96 hours.the incidence of vomiting was 1.7% in the combination group whereas it was 6.8% in the group that received palonosetron alone. complete response (i.e no nausea and vomiting) to the drug under study was similar in both groups. There was no significant difference between the group that received palonosetron and dexamethasone combination mixture and the group that received only palonosetron.

Chun HR et al., in a randomized double blinded study, evaluated the efficacy of palonosetron in the prevention of nausea and vomiting.In this placebo controlled study,204 subjects who underwent elective surgery were randomly divided into two groups consisting of 102 subjects each.one group received palonosetron 0.075mg and the other group received

normal saline. patients were observed for a period of 72 hours for the incidence of nausea and vomiting, severity of nausea and the use of rescue antiemetic. The incidence of post operative nausea and vomiting was 33% in palonosetron group and 47% in placebo group during 0-24 hours and when observed for a period of 72 hours, the incidence of post operative nausea and vomiting is 33% in palonosetron group and 52% in placebo group. The incidence of nausea was also lower in palonosetron group than the placebo group. The results obtained from the study proved that palonosetron significantly reduced the incidence of nausea and vomiting when compared to the placebo group.

Laha et al., evaluated the antiemetic effect of intravenous Palonosetron versus intravenous Ondansetron in patients undergoing laparoscopic cholecystectomy. In this randomized single blinded study consisting of 49 subjects in each group ,the incidence of post operative nausea and vomiting was observed over a period of 24 hours. The incidence at 0,2,6 and 24 hours was noted.The nausea score was comparable in the two

groups. complete response was seen in 28.6% patients in palonosetron group and 32.7% in Ondansetron group. The efficacy of palonosetron is comparable to ondansetron in the prevention of post operative nausea and vomiting.

Sarbari swaika et al., did a randomized double blinded study to compare the antiemetic effect of Ondansetron, Palonosetron and Ramosetron in patients undergoing laparasocopic cholecystestomy. This study was done in a group of 87 female patients randomly divided into three groups consisting of 29 subjects each.The three study groups were allocated to recive Ondansetron 8mg, Palonosetron 0.075mg and Ramosetron 0.3mg. The drug was administered at the end of surgery just before extubation. The patients were observed over a period of 24 hours and the complete response to nausea, vomiting and the requirement of rescue antiemetic was compared. It was found that the incidence of complete response was 65.5 % Ramosetron and 37.9% for Palonosetron and 34.5 % for Ondansetron. Hence a singinficant difference between

the three groups was noted. When Ramosetron was compared with Palonosetron, it was found that Ramosetron is superior to Palonosetron in the prevention of nausea and vomiting.It was concluded from the study that 0.3mg of Ramosetron is better than 0.07mg of Palonosetron and 8mg Ondansetron in preventing the nausea and vomiting in the post operative period.

Ahmed M AbdEI et al., conducted a study to compare the efficacy of Palonosetron versus Ondansetron in the prevention of post operative nausea and vomiting in patients undergoing middle ear surgery.60 patients scheduled to undergo middle ear surgery were randomly divided into two groups consisting of 30 subjects each and they were allocated to receive Ondansetron 4mg intravenously and Palonosetron 0.25mg intravenously.The drug was administered just before the induction of anaesthesia and complete response to nausea, vomiting , severity of nausea and the requirment of rescue antiemetic was noted. It was observed that 28 patients in Palonosetron group had complete response when compared to 22 patients in Ondansetron group. 4

patients in Palonosetron group required rescue antiemetic,whereas there was no requirement of antiemetic in Palonosetron group.The severity of nausea score was also less in Palonosetron group.It was concluded that Palonosetron was superior to Ondansetron with minimal side effects.

MATERIALS AND METHODS.

This was a randomized single blinded interventional study conducted at Government Kasturba Gandhi Hospital for Women and Children, Madras Medical College, Chennai.

Instituition Ethical committee approval was obtained before proceeding the study. Informed written consent was obtained from all the 100 patients who were scheduled to undergo elective laparoscopic gynaecological surgery.Information about the study type,the drug,its benefits and side effects were clearly explained and willingness of the patient to participate in the study was documented.

The Inclusion Criteria

Age more than 18 years and above,

ASA PS 1&2.

Patients undergoing elective surgery.

Mallampati score 1&2

patients who are willing to undergo the study

Patients who have given written informed consent.

The Exclusion Criteria

Patients posted for emergency surgery.

Lack of written informed consent.

Pregnant female.

History of seizures and any neurological deficit.

History of motion sickness.

History of nausea and vomiting 24hrs prior to surgery.

Patients with history of significant cardiovascular disease or rhythm disturbance, liver, renal and endocrine abnormalities.

METHOD

Study population of 100 patients were randomly assigned using statistical software into two groups of 50 each.Patients were blinded about the study drug. Group

O received 2 ml of 4mg of Ondansetron and Group P received 2 ml of 0.075 mg of Palonosetron intravenously before the induction of Anesthesia. The drug was administered by the Anaesthesiologist who was involved in the assessment of the patient. In all the patients undergoing study, standard anesthesia technique was followed.

Study subjects were preloaded with 15 ml/kg Ringer Lactate intravenously.All patients received premedication with Injection glycopyrrolate 0.004mg/kg and Injection fentanyl 2 mcg/kg intravenously 30 mins prior to induction. The study drug was administered according to the group. Anesthesia was induced with Injection thiopentone at a dose of 5 mg/kg .Intubation was facilitated with Injection atracurium 0.05 mg/kg.Single use polyvinylchloride(PVC) endotracheal tube was used for intubation.Anaesthesia was maintained with Oxygen and Nitrous oxide mixture in a ratio of 1:3 and the volatile anaesthetic used for maintenance was sevoflurane,the concentration of which

was titrated between 1-2% according to the depth of Anesthesia.

Intraoperatively muscle relaxation was maintained with Injection Atracurium 0.01 mg/kg.Hemodynamic stability in the intra operative period was monitored with heart rate, electrocardiogram, blood pressure, pulse oximeter and end tidal CO2 monitor.

Intraoperatively, the gas used for insufflation during laparoscopy was carbon dioxide. Intra abdominal pressure was maintained between 14-16mmHg.heart rate and blood pressure was maintained within 20% of the preoperative values. Neuromuscular blockade was reversed with Injection Neostigmine 0.04mg/kg and Injection Glycopyrrolate 0.004 mg/kg. In the immediate post operative period patient was shifted to recovery room for monitoring of vitals which includes heart rate,electrocardiogram and oxygen saturation.

Patients were followed up for the incidence of nausea and vomiting immediately after extubation, during 0-2 hours,2-24 hours and then over a period of 24-48

hours.patients were asked whether they had nausea and vomiting and other complaints like headache, dizziness and constipation were also recorded.

Data obtained were analyzed and the statistical results were obtained using SPSS software.

OBSERVATION AND RESULTS

Study population of 100 patients undergoing elective laparoscopic gynaecological surgeries were randomly divided into two groups.50 patients were allotted to group O receiving ondansetron and 50 patients were allotted to group P receiving palonosetron.

Statistical analysis was done using SPSS package version 17 for windows.To compare intergroup differences, student's T test was used and for categorical variables chi square or fisher's exact test was used .A P value less than 0.05 was considered to be statistically significant.

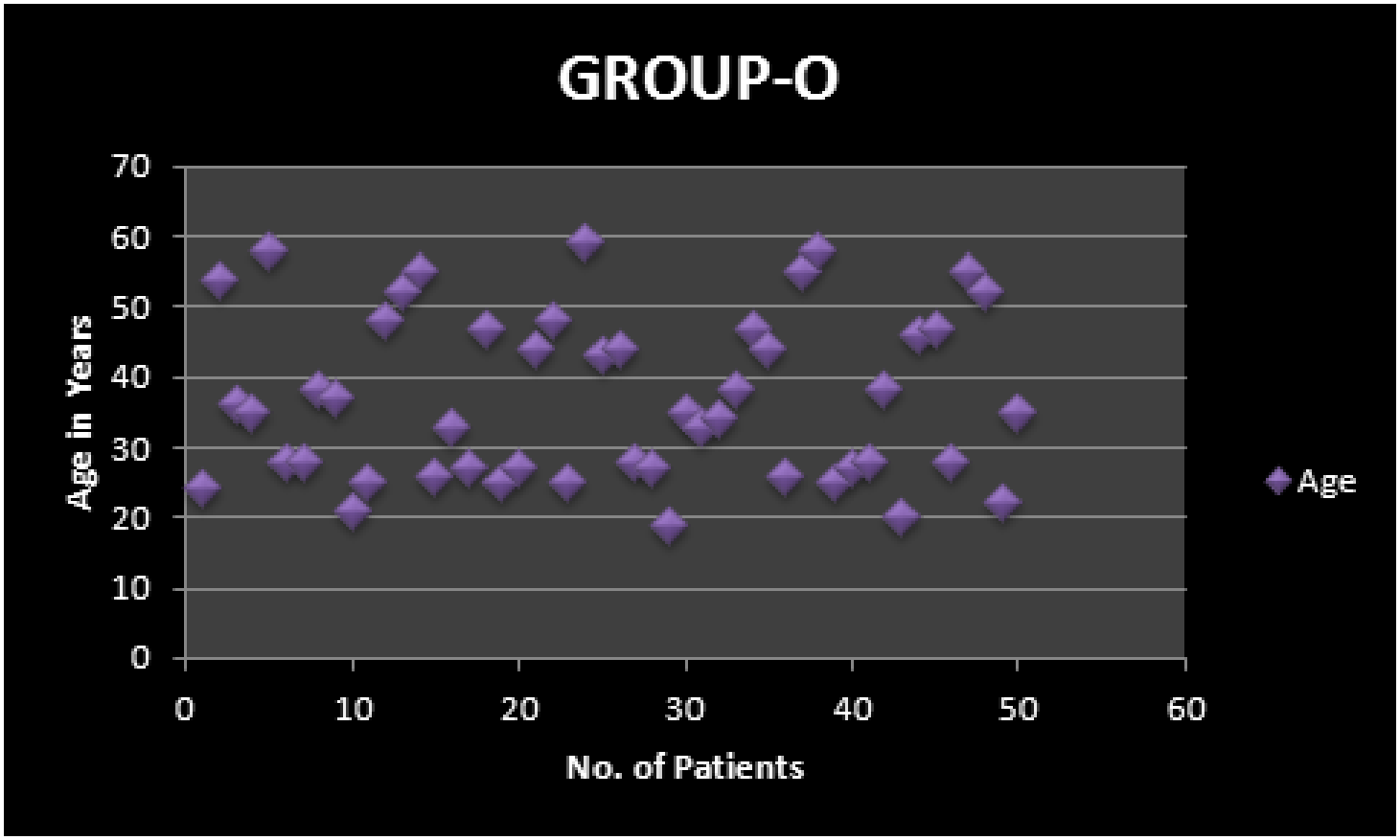
AGE DISTRIBUTION

Female patients aged 18 years and above were included in this study.

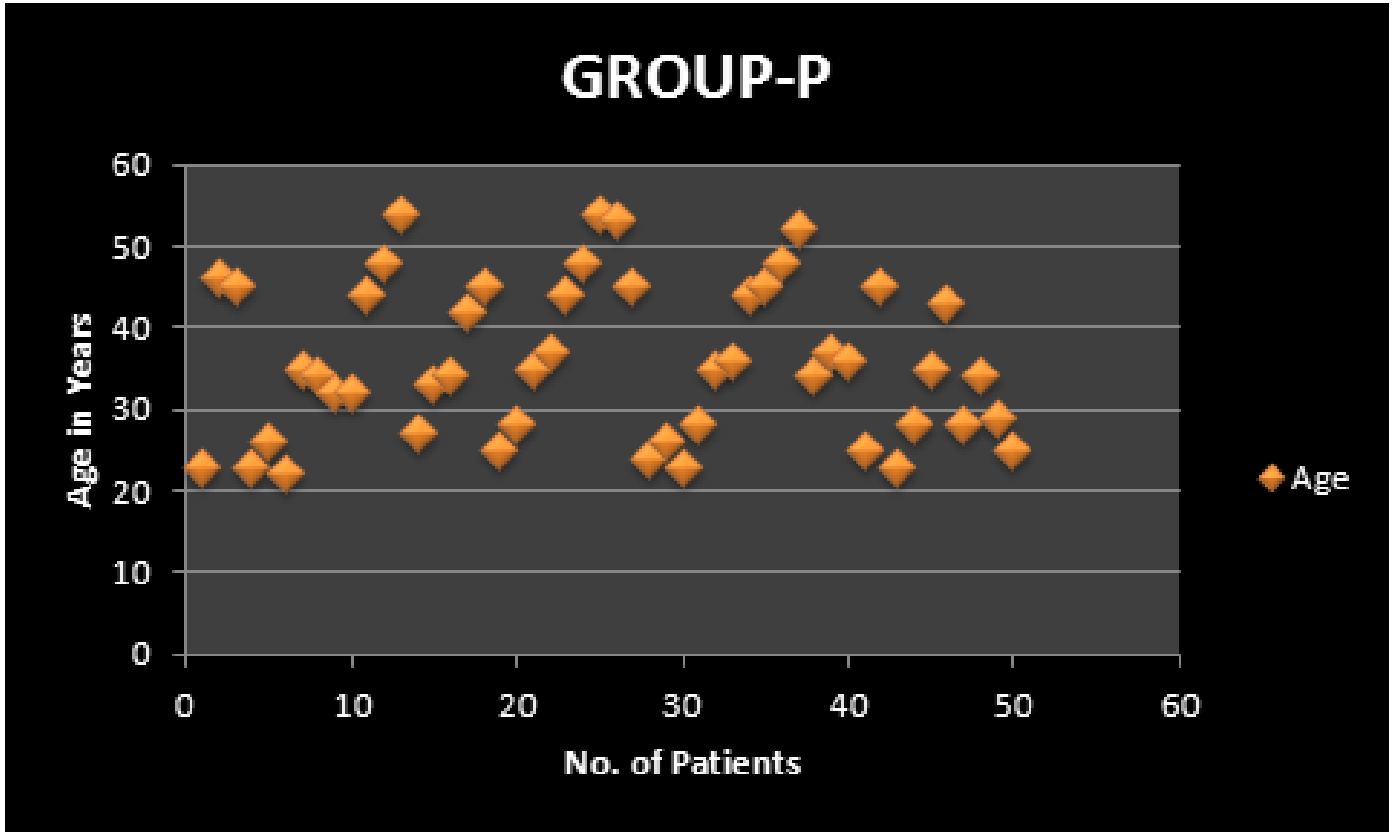
AGE (YEARS)				
Group	**N**	**Mean**	**Std. Deviation**	**P VALUE**
O	50	37.08	11.803	0.596
P	50	35.94	9.513	

Patients under 40 years of age comprised the majority of study population. The P value is 0.596 and there was no statistically significant difference in the age of the patients between the two study groups.

The following chart shows age distribution in ondansetron group.


GROUP-O
70
60
50
40
30
20
10
0
Age in Years
0
10
20
30
40
50
60
No. of Patients
Age

The following chart shows age distribution in palonosetron group.

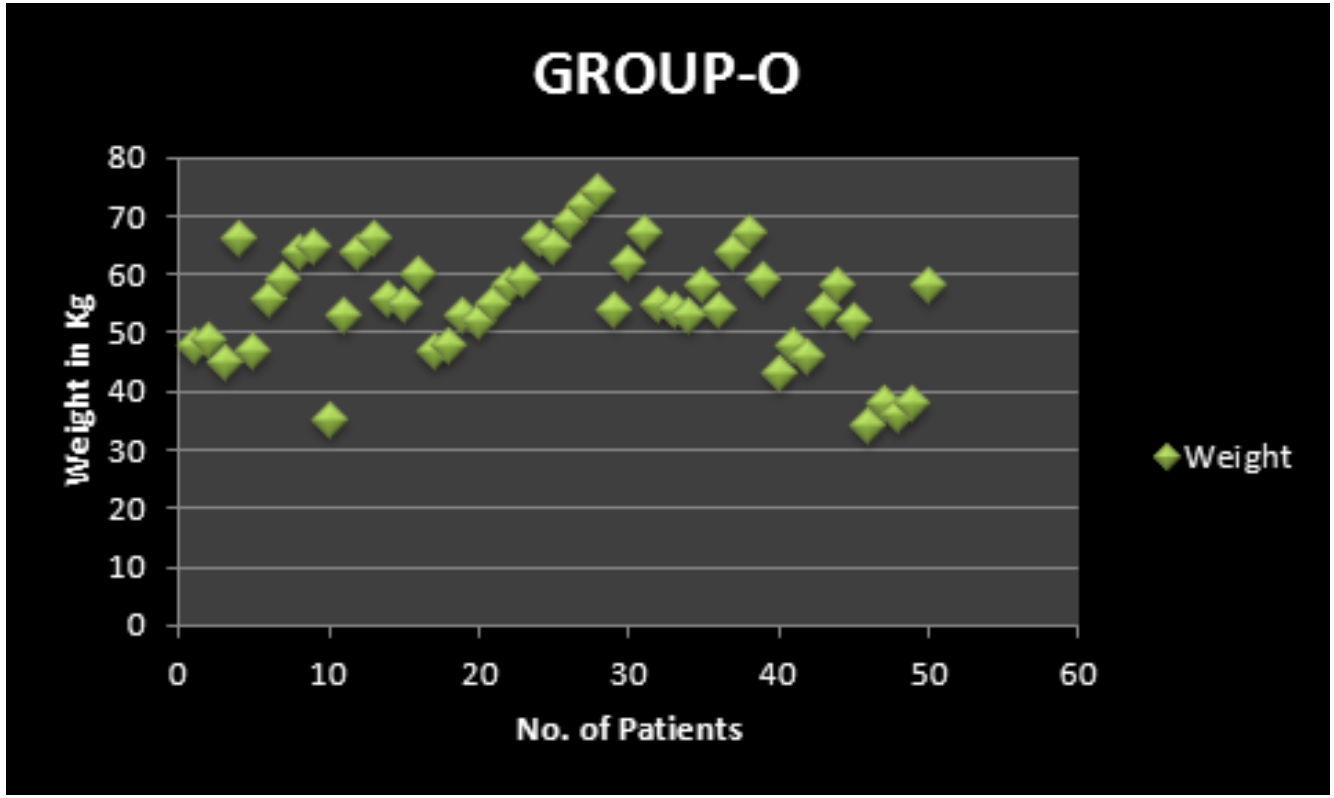


WEIGHT DISTRIBUTION

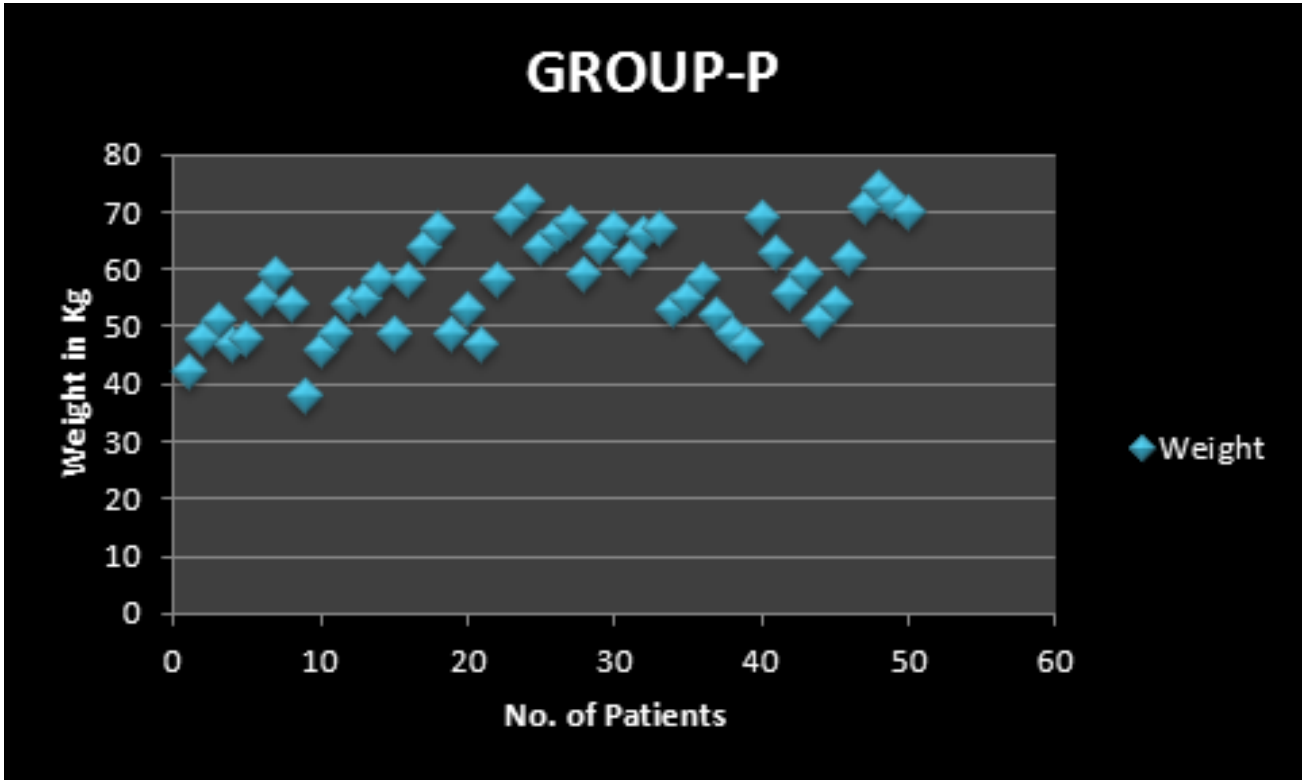
WEIGHT(Kg)			
Group	**Mean**	**Standard deviation**	**P value**
O	55.16	9.63	0.162
P	57.76	8.79	

The average distribution of weight in ondansetron group is 55.16 and palonosetron group is 57.16.The P value based on student's T test is 0.162 which is not statistically different. The two groups were comparable in weight distribution.

The following chart shows the distribution of weight in ondansetron group.



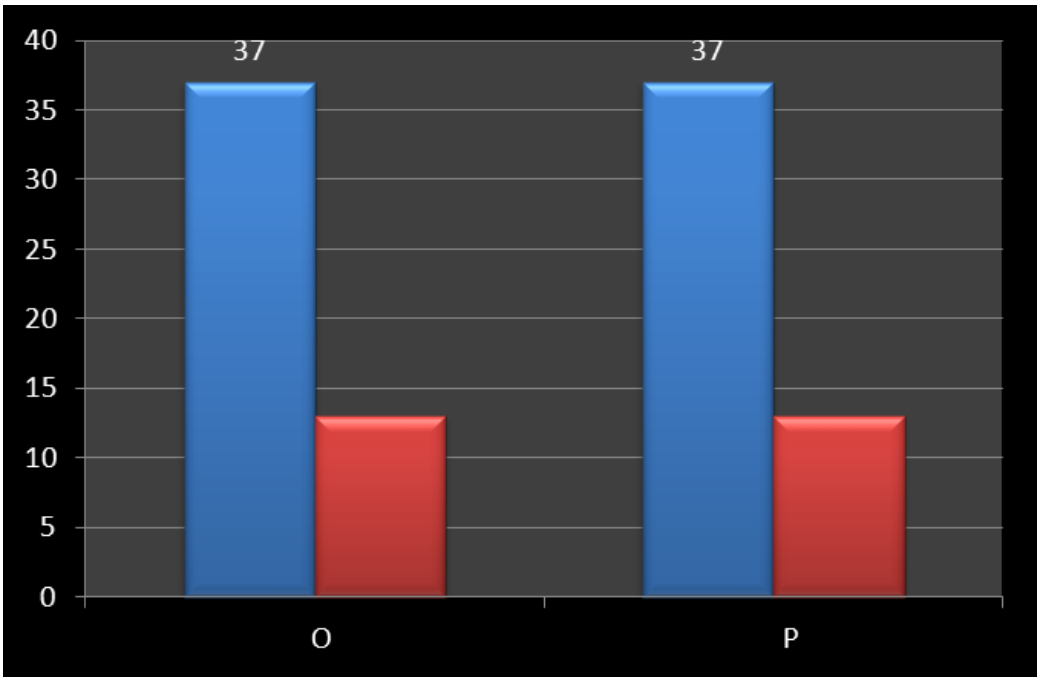
The below chart shows the distribution of weight in Palonosetron group.



ASA PHYSICAL STATUS

Patients belonging to the ASA physical status 1&2 were included in the study group.

GROUP	PS 1	PS 2	P VALUE
O	37	13	1.000
P	37	13	



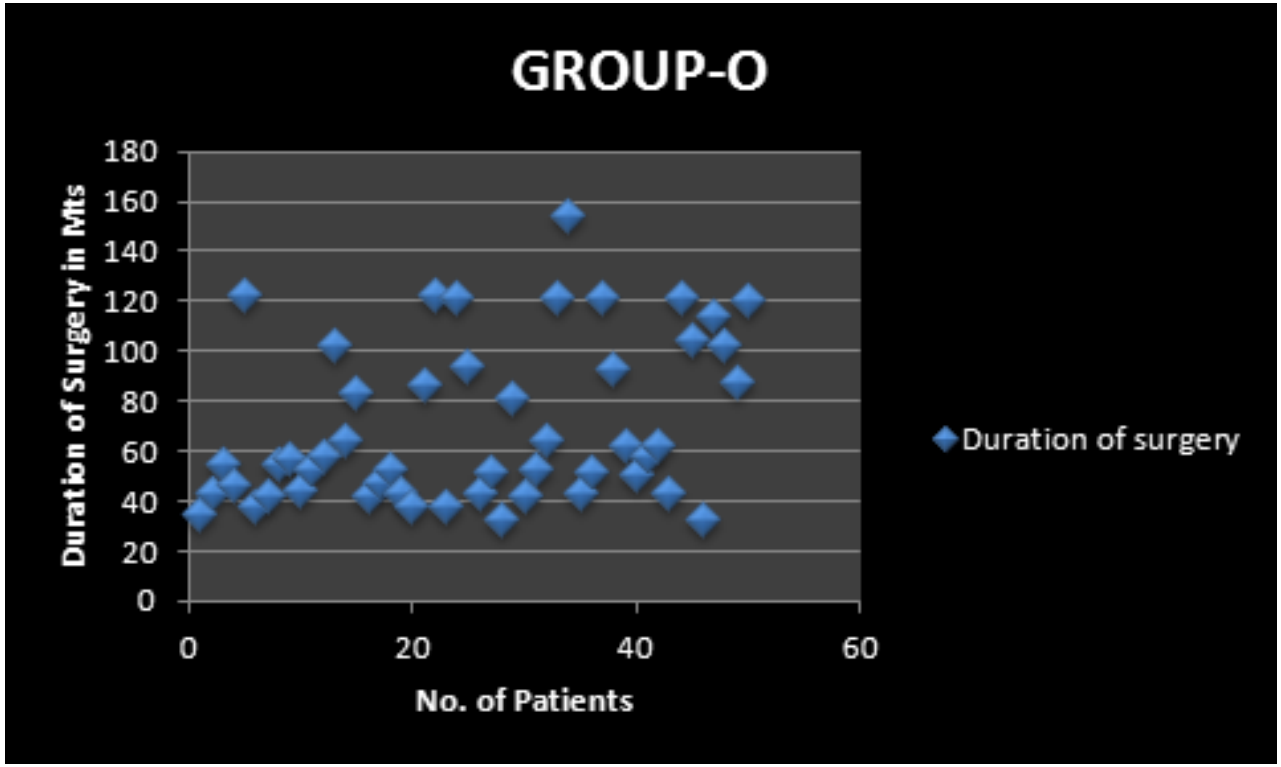
Based on T test the p value is 1.000.Hence there is no statistical difference between the two groups and they are comparable.

DURATION OF SURGERY

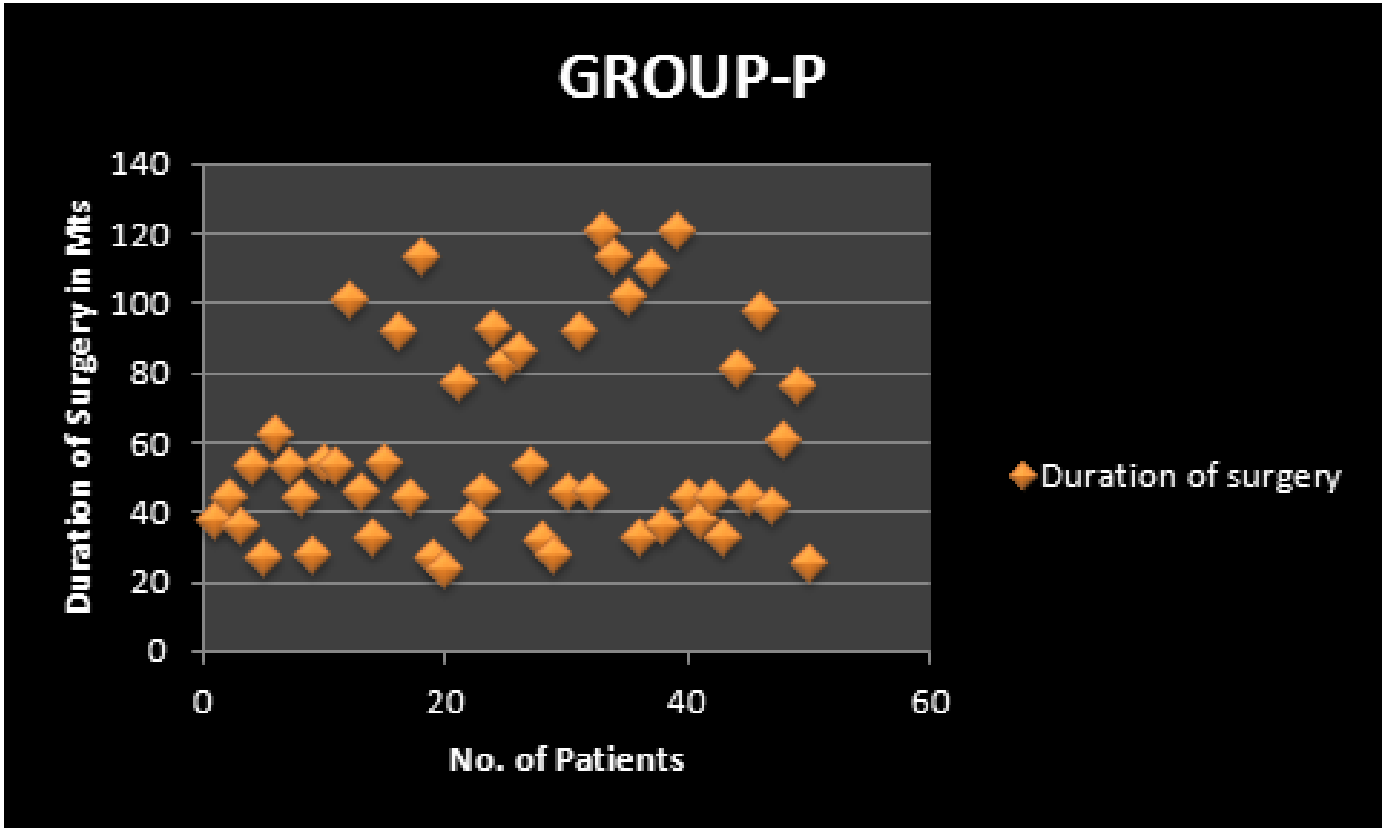
The mean value of patient weight in ondansetron group is 69.86 and 59.36 in palonosetron group.Based on T test, P value is 0.089.There is no statistical difference between the two groups and hence they are comparable in terms of duration of surgery.

DURATION OF SURGERY			
Group	**Mean**	**Standard Deviation**	**p Value**
O	69.86	32.07	0.089
P	59.36	28.92	

The following chart shows the distribution of duration of surgery (minutes) in ondansetron group.



The following chart shows the distribution of duration of surgery (minutes) in Palonosetron group.

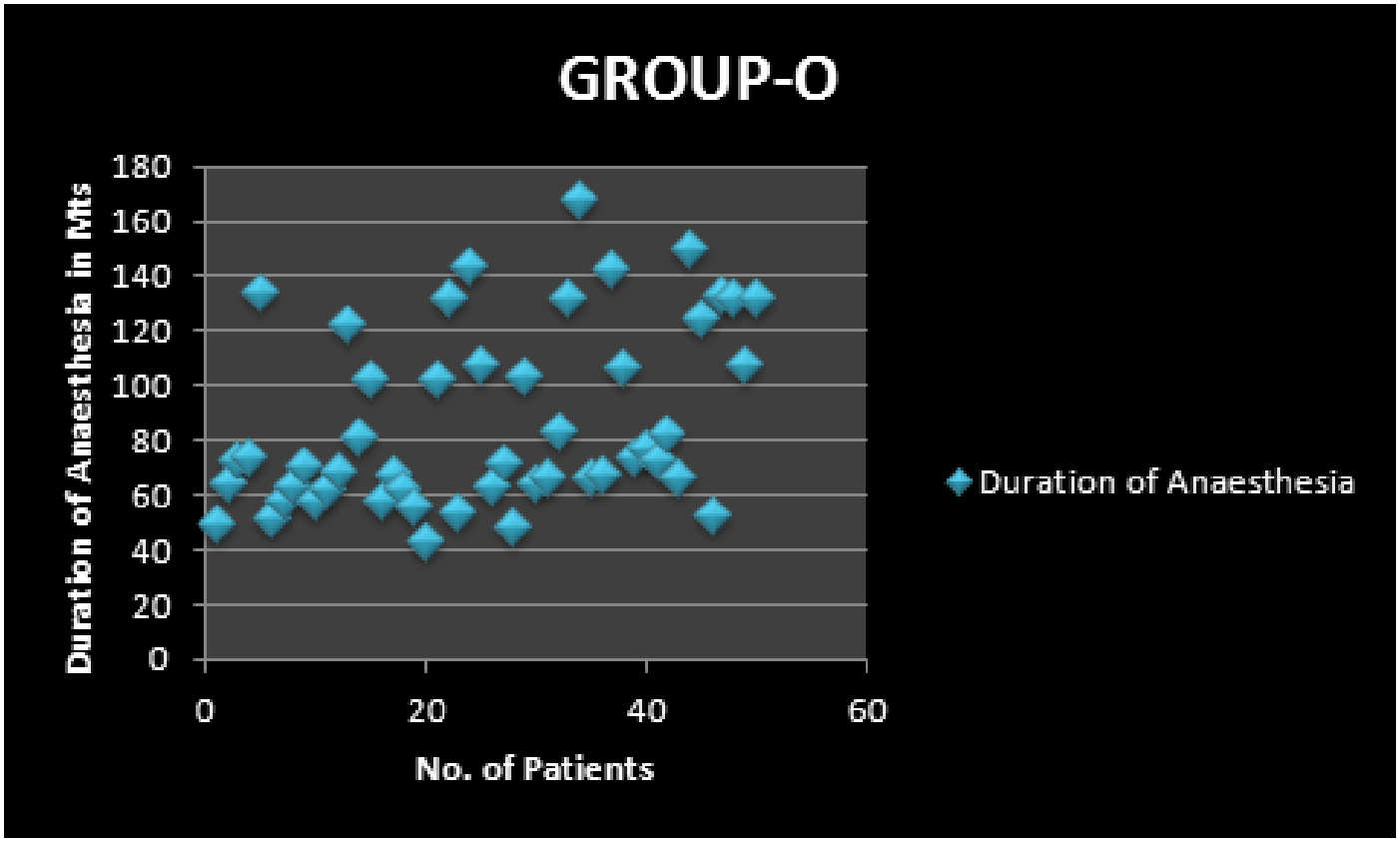


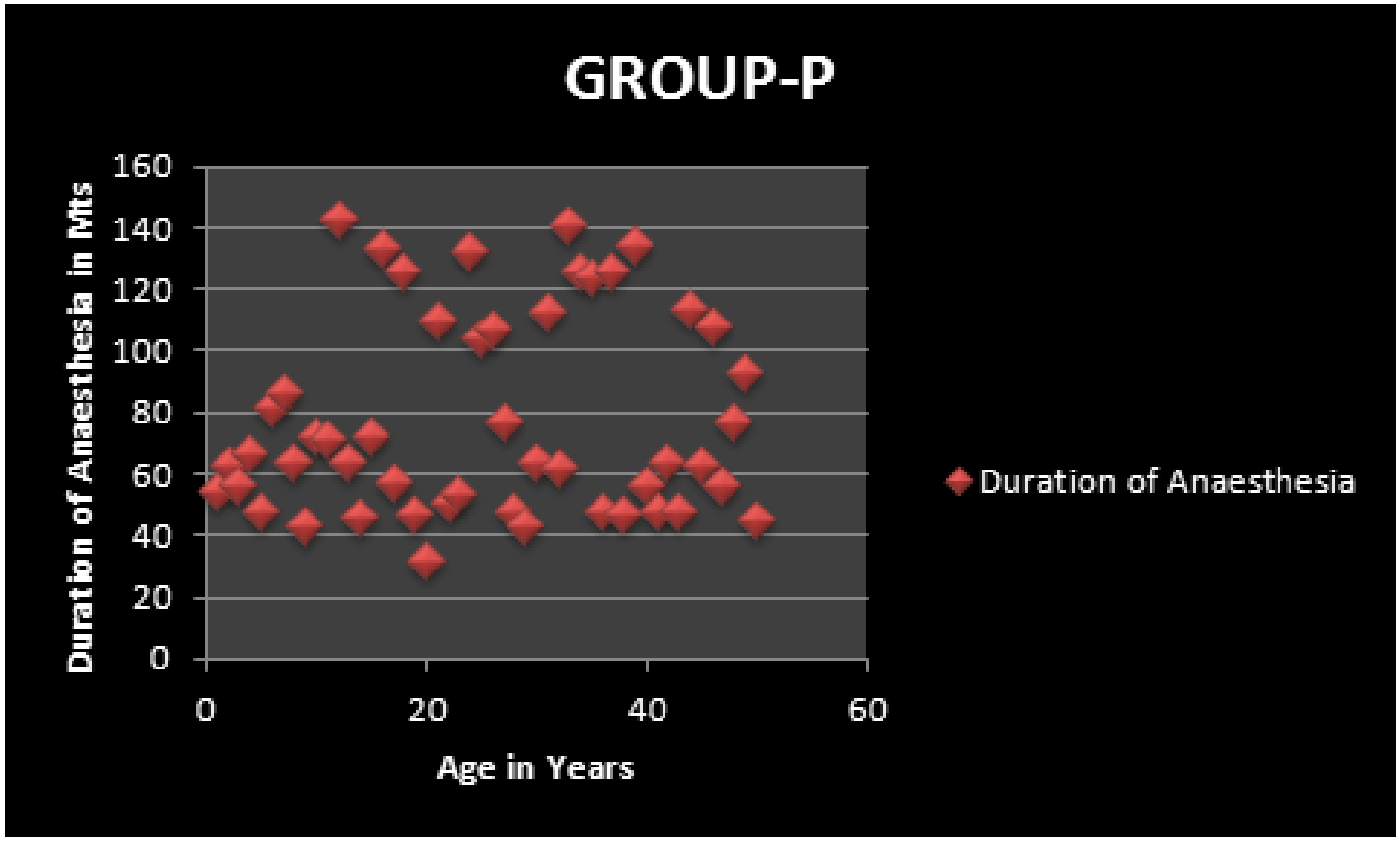
DURATION OF ANAESTHESIA

DURATION OF ANAESTHESIA			
Group	**Mean (minutes)**	**Standard deviation**	**p value**
O	86.92	32.91	0.182
P	78.16	32.33	

Based on T test for equality of means the P value was found to be 0.182. There was no statistical significance between the two groups and the duration of anaesthesia was comparable between two groups.

The following charts shows the distribution of duration of anaesthesia in ondansetron group.





The above charts shows the distribution of duration of anaesthesia in palonosetron group.

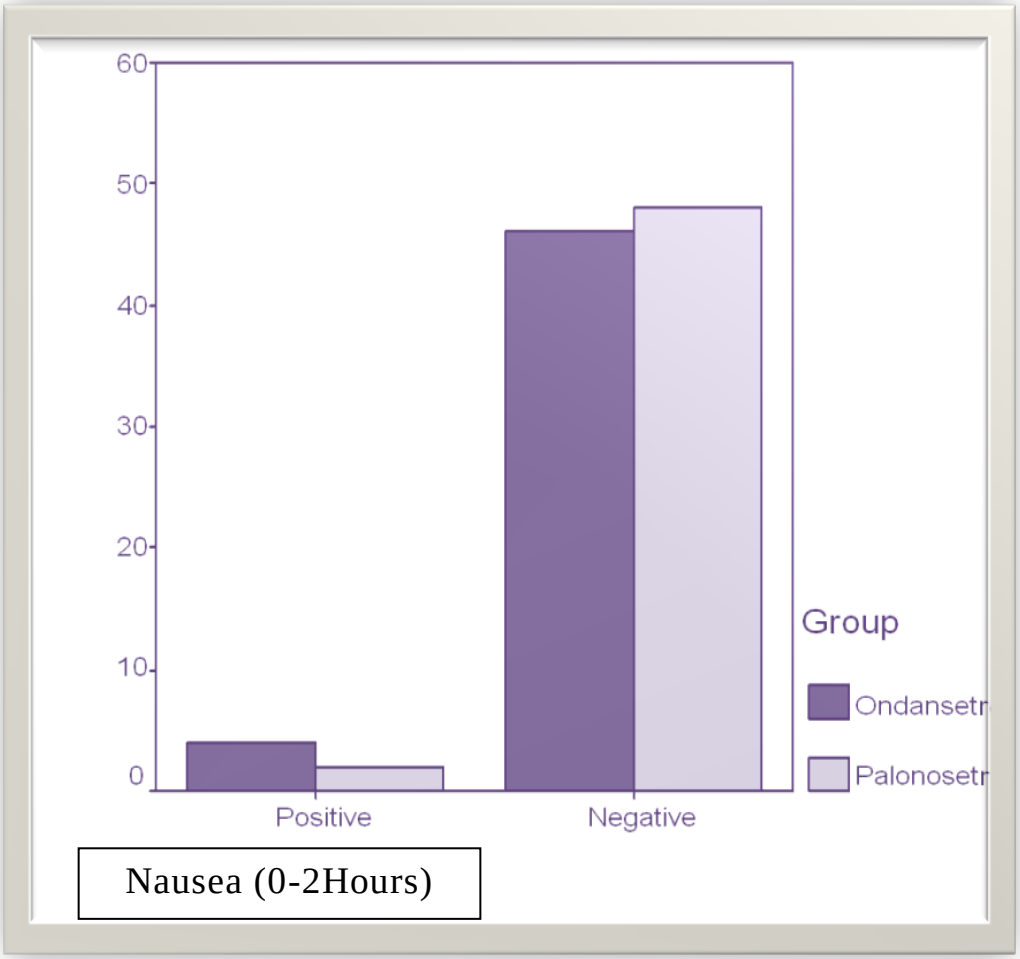
NAUSEA(0-2 HOURS)

The incidence of nausea was 8 % in the ondansetron group when compared to 4% in the palonosetron group.with respect to the incidence of nausea in the first two hours of the post operative period,patients in O (ondansetron) group had no significant difference in the incidence of nausea when compared to patients in the P (palonosetron) group with a P value of 0.395 by chi – square test.

Comparision of incidence of nausea (0-2 HOURS) (chi – square test)

NAUSEA(0-2 HOURS)				
GROUP	**0**	**P**	**TOTAL**	**P VALUE**
+	4 (8%)	2 (4%)	6 (6%)	0.395
-	46 (48.9%)	48 (51.1%)	94 (94%)	

The following chart compares the incidence of nausea in the first two hours between the two study groups.



Nausea (0-2Hours)

NAUSEA (2-24 HOURS)

Three patients in group O reported nausea and there was no incidence of nausea in the palonosetron group in 2-24 hrs.

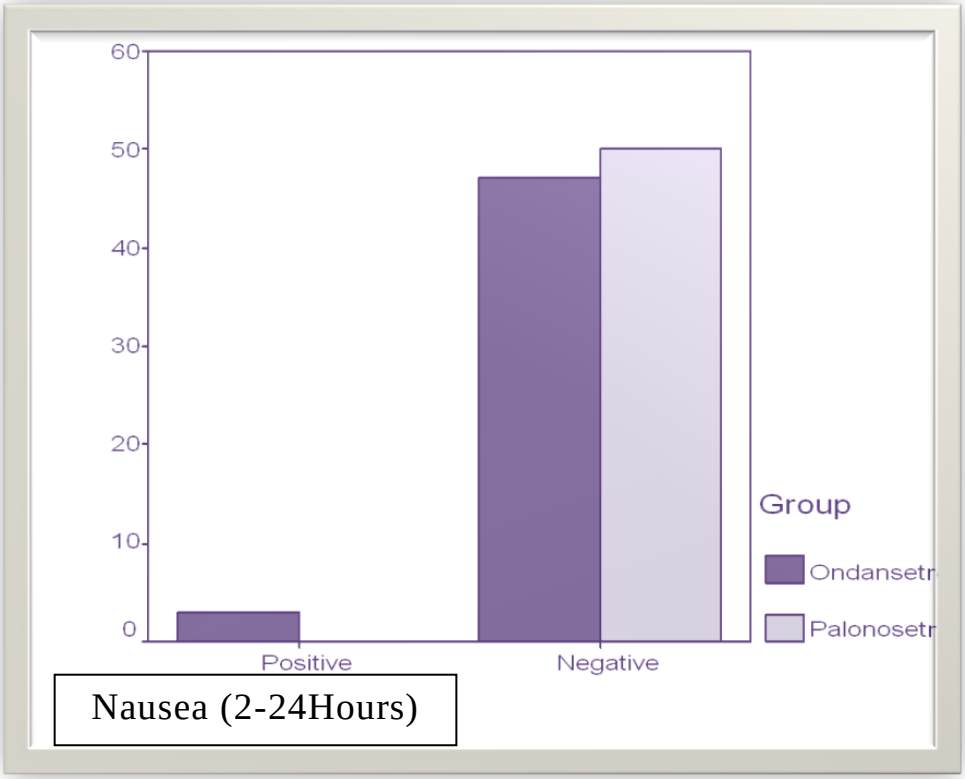
Comparision of nausea in 2-24 hours. (chi-square test)

NAUSEA (2-24 HOURS)			
GROUP	**O**	**P**	**P VALUE**
+	3 (6%)	0 (0%)	0.039
_	47 (94%)	50 (100%)	

The P value by chi-square test was 0.039 .

The difference in the incidence of nausea over a period of 2-24 hours was statistically significant with the incidence of 6% nausea in the ondansetron group compared to palonosetron group with no incidence of nausea.

The below chart compares the incidence of nausea during 2-24 hours between the two groups.



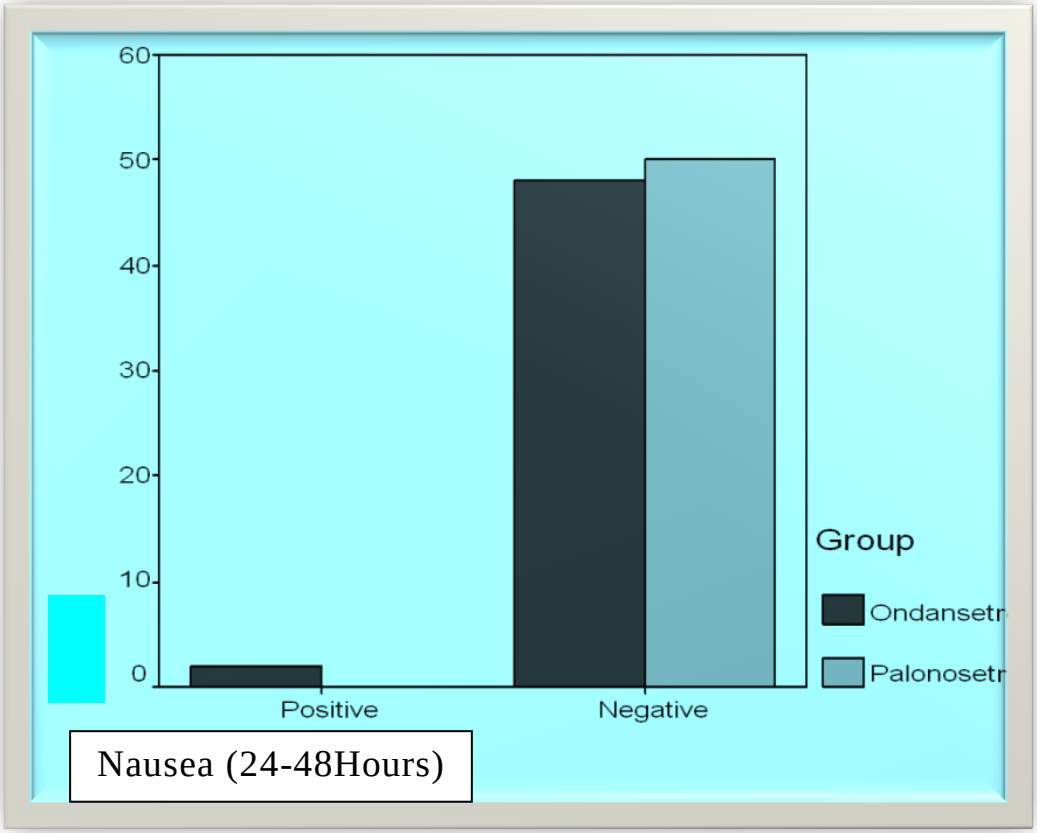
Nausea (2-24Hours)

NAUSEA(24-48 HOURS)

With the incidence of 4% (2 patients) nausea in ondansetron group compared to nil incidence of nausea in palonosetron group over a period of 24-48 hours, the P value was found to be 0.093 by chi-square test which implies that there is no statistically significant difference between the two groups.

COMPARISION OF NAUSEA (24-48 HOURS)

CHI SQUARE TEST			
GROUP	**O**	**P**	**P VALUE**
+	2 (4%)	0 (0%)	0.093
-	48 (96%)	50 (100%)	

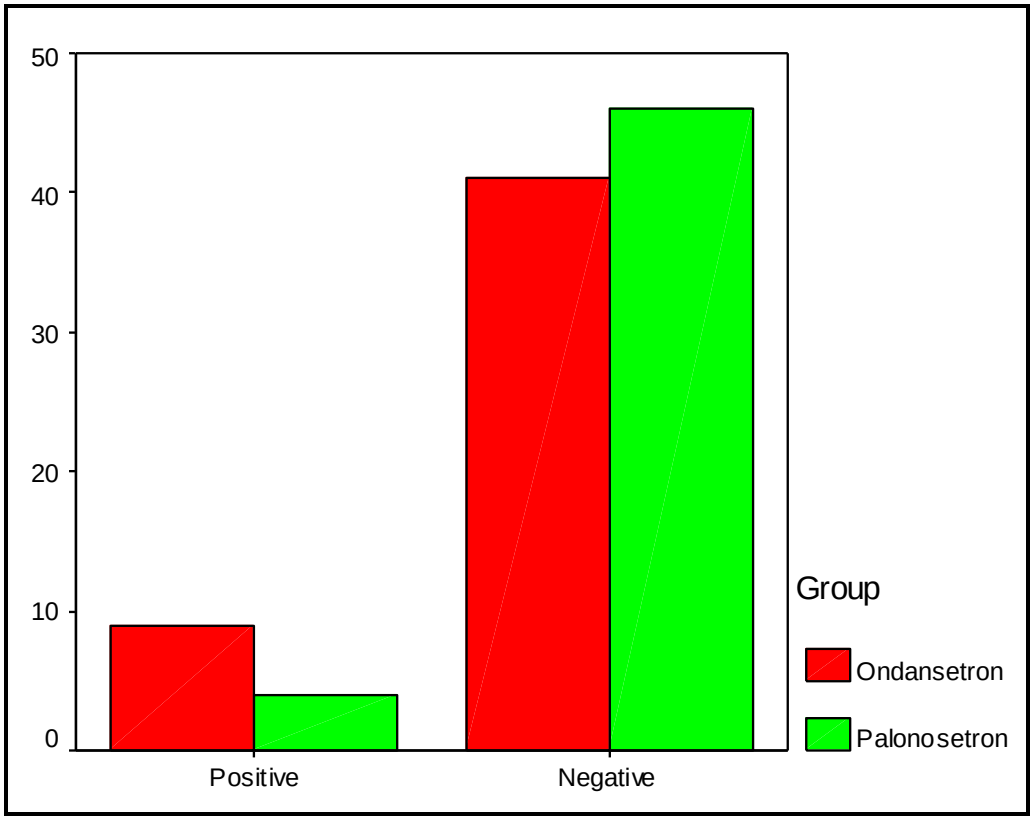


The above chart shows the comparison of the incidence of nausea (24 to 48 hours) between the two groups.

VOMITING (0-2 HOURS)

The incidence of vomiting in ondansetron group is 18% (9 Patients) and 8% (4 Patients) in palonosetron group. BY statistical analysis using chi-square test the p value was found to be 0.137 and hence there is no statistical difference in the incidence of vomiting in the immediate two hours following surgery.

COMPARISON OF VOMITING(0 TO 2 Hours)			
Group	**O**	**P**	**P VALUE**
+	9 (18%)	4 (8%)	0.137
-	41 (82%)	46 (92%)	



(Vomiting 0-2 Hours)

The above chart compares the incidence of vomiting in 0-2 hours between the two groups.

VOMITING (2 TO 24 HOURS)

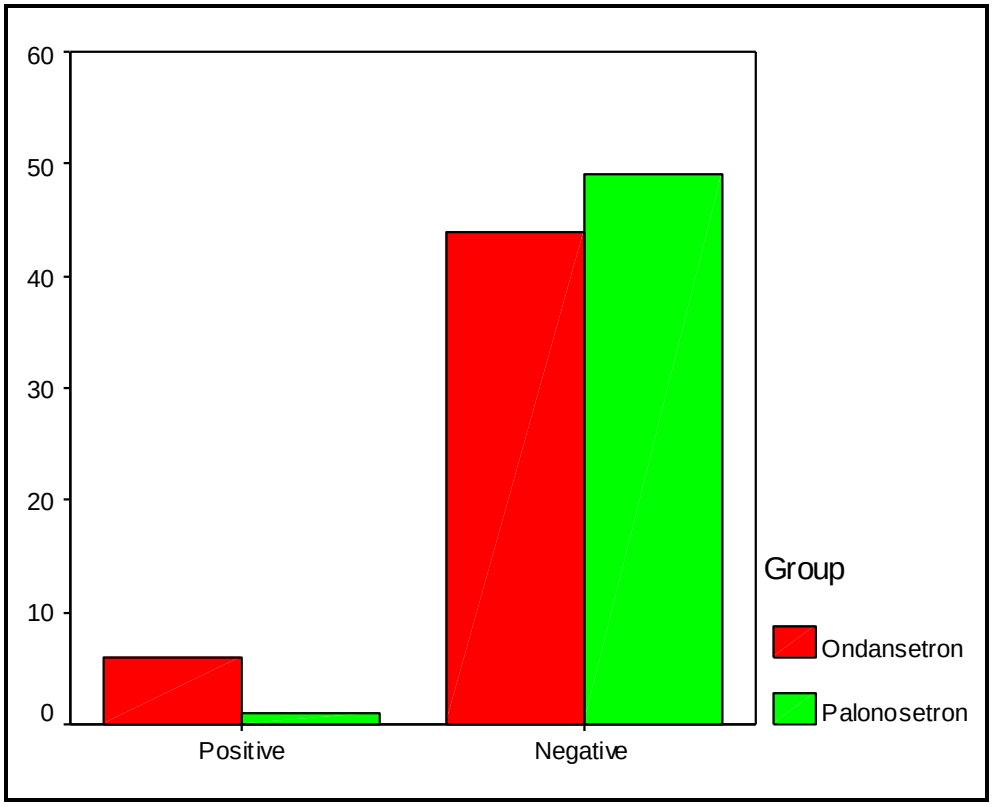
With respect to the incidence of vomiting in 2 to 24 hours, it was found that group O had 12% incidence (6 Patients) Whereas group P had 2% incidence (1 Patient). The difference in the incidence of vomiting between the two groups was significant with the P value of 0.050 (Chi – Square test).

COMPARISON OF VOMITING (2 TO 24 HOURS):

(CHI – SQUARE TEST)

VOMITING (2 TO 24 HOURS)			
GROUP	**O**	**P**	**P VALUE**
+	6 (12%)	1 (2%)	0.050
-	44 (88%)	49 (98%)	

The below chart compares the incidence of vomiting (2 – 24 hours) between the two groups.



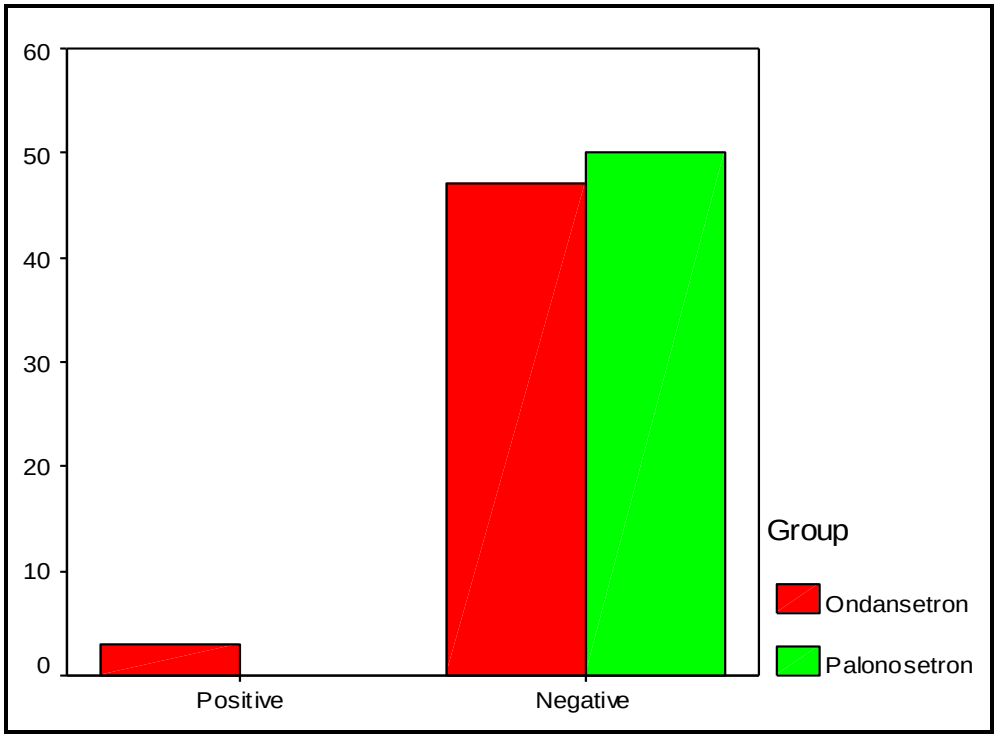
(Vomiting 2-24 Hours)

VOMITING (24 – 48 HOURS)

In the analysis of incidence of vomiting over a period of 24 to 48 hours, it was found that the incidence is 6% in ondansetron group compared to nil incidence of vomiting in palonosetron group. The P value was found to be 0.039 and statistically significant difference between the two groups was observed.

COMPARISON OF VOMITING (24 – 48 HOURS)

VOMITING (24 TO 48 HOURS)			
GROUP	**O**	**P**	**P VALUE**
+	3(6%)	0 (0%)	0.039
-	47 (94%)	50 (100%)	



(Vomiting 24-48 Hours)

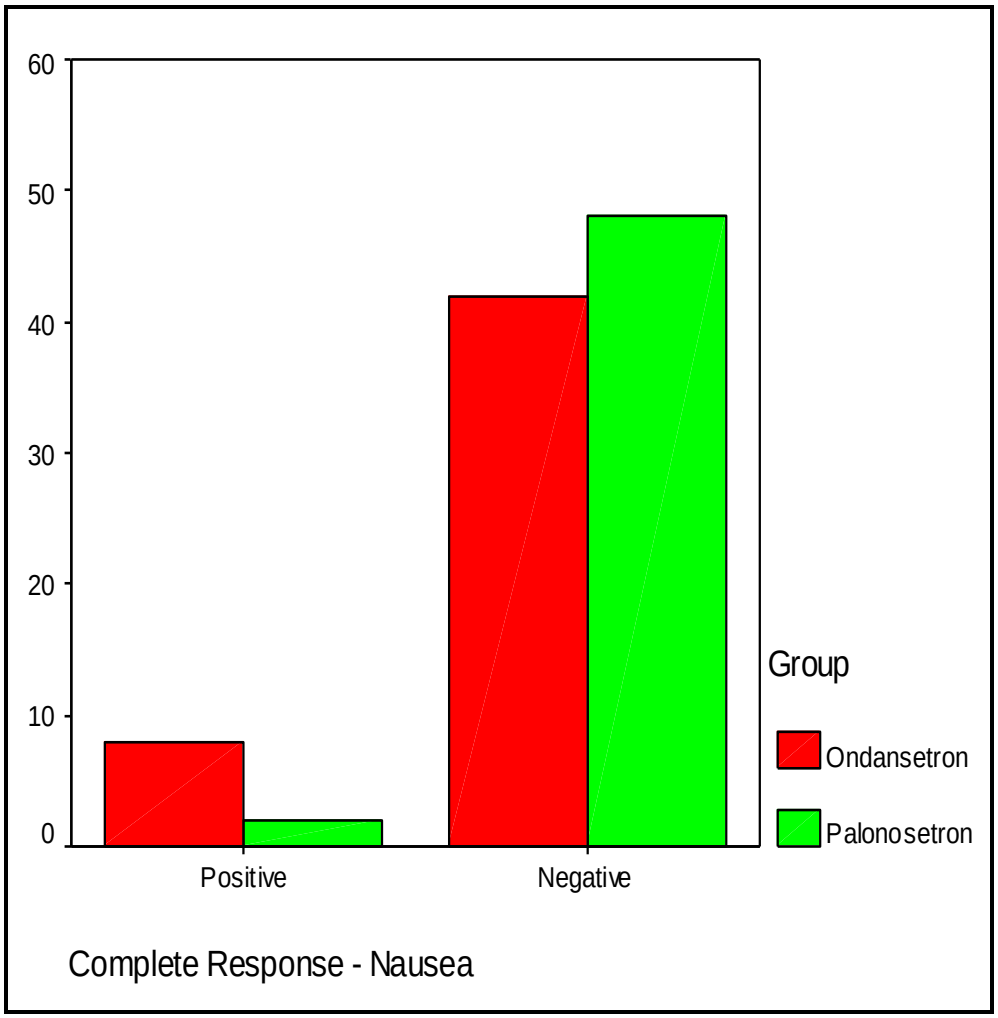
The above chart compares the incidence of vomiting (24 – 48 hours) between the two groups.

COMPLETE RESPONSE TO NAUSEA

Complete response to nausea was found to be 84% in ondansetron group when compared to 96% in palonosetron group. With the P value of 0.046% ,significant difference in complete response to nausea was found between the two groups.

COMPLETE RESPONSE TO NAUSEA

COMPLETE RESPONSE (NAUSEA)			
GROUP	**O**	**P**	**P VALUE**
+	8 (16%)	2 (4 %)	0.046
-	42 (84 %)	48 (96%)	



The chart above shows the comparison of complete response to nausea between the ondansetron and palonosetron group.

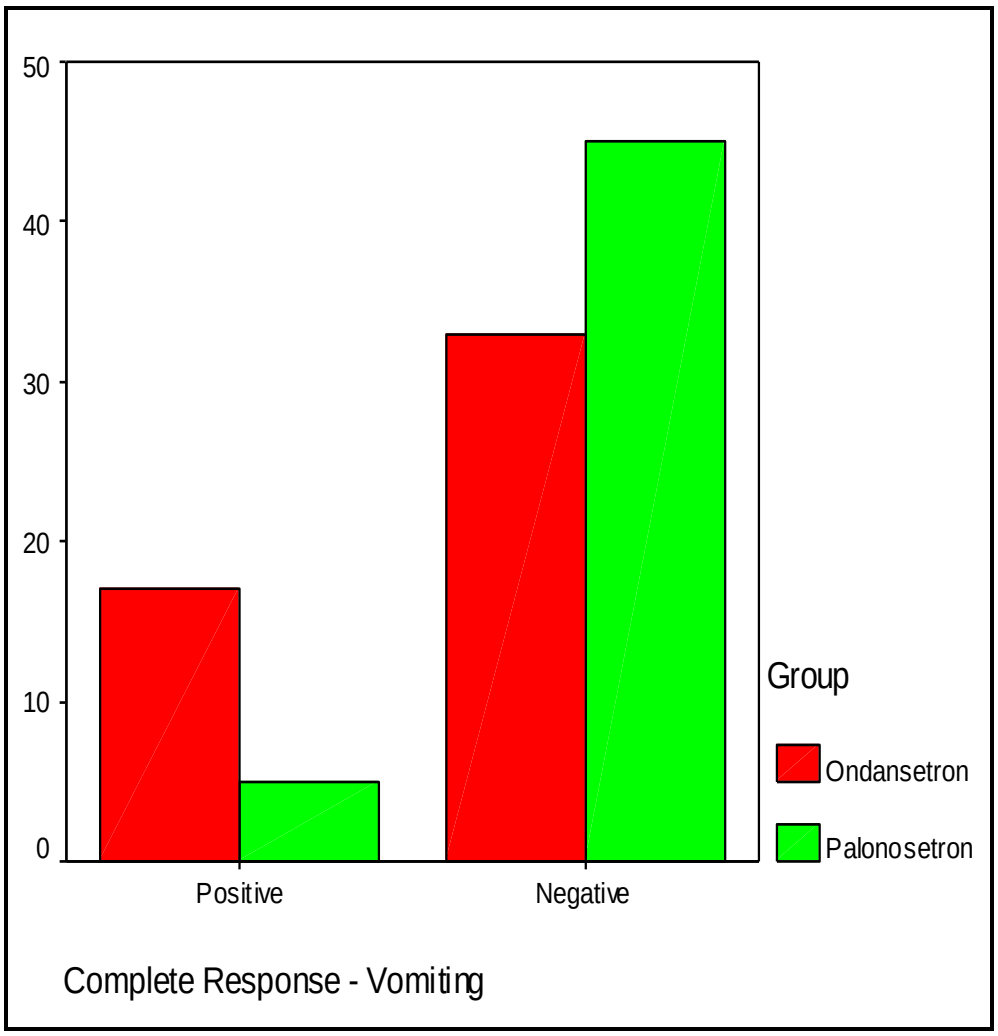
COMPLETE RESPONSE TO VOMITING

In comparing the complete response to vomiting, it was found that complete response was 66% (17 Patients) in ondansetron group and it was 90% (5 Patients) in palonosetron group. The P value by chi - square test was found to be 0.04 and it was a highly significant statistical difference between the two groups.

COMPARISON OF COMPLETE RESPONSE TO VOMITING

(CHI – SQUARE TEST)

COMPLETE RESPONSE TO VOMITING			
GROUP	**O**	**P**	**P VALUE**
+	17 (34%)	5(10 %)	0.004
-	33 (66 %)	45 (90%)	

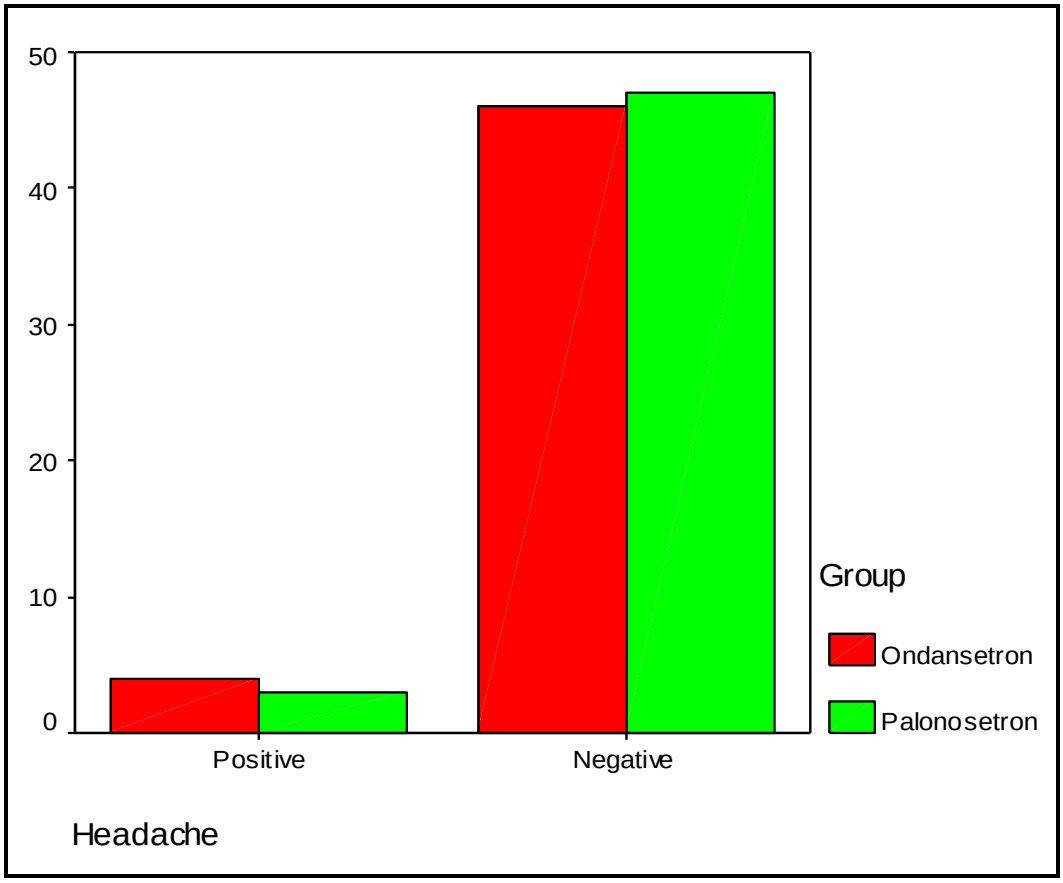


The chart above shows the comparison of complete response to vomiting between the ondansetron and palonosetron group.

HEADACHE

The incidence of headache was 8% (4 Patients) in ondansetron group and 6% (3 Patients) in palonosetron group. The two groups were comparable with P value of 0.695.

HEADACHE			
GROUP	**O**	**P**	**P VALUE**
+	4 (8%)	3 (6%)	0.695
-	46 (92%)	47 (94%)	

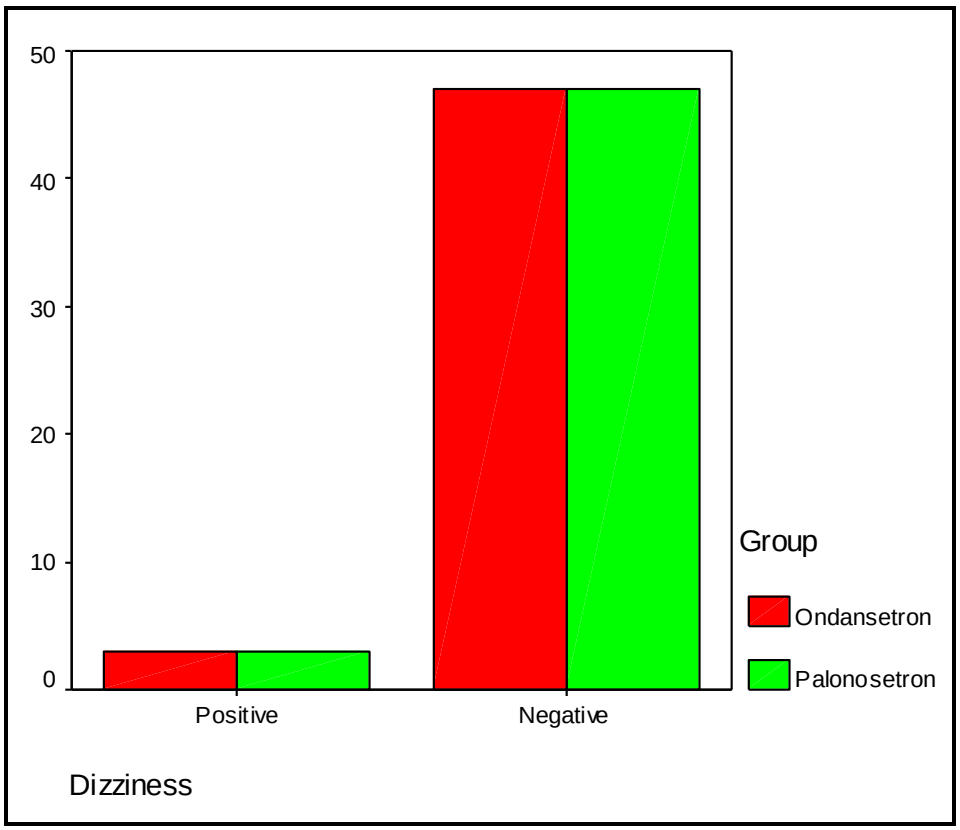


The chart above shows the comparison of the incidence of headache between the ondansetron and palonosetron group.

DIZZINESS

The incidence of dizziness was 6% (3 Patients) in both groups and there is no difference between the two groups with the P value of 1.000

DIZZINESS			
GROUP	**O**	**P**	**P VALUE**
+	3 (6%)	3 (6%)	1.000
-	47 (94%)	47 (94%)	

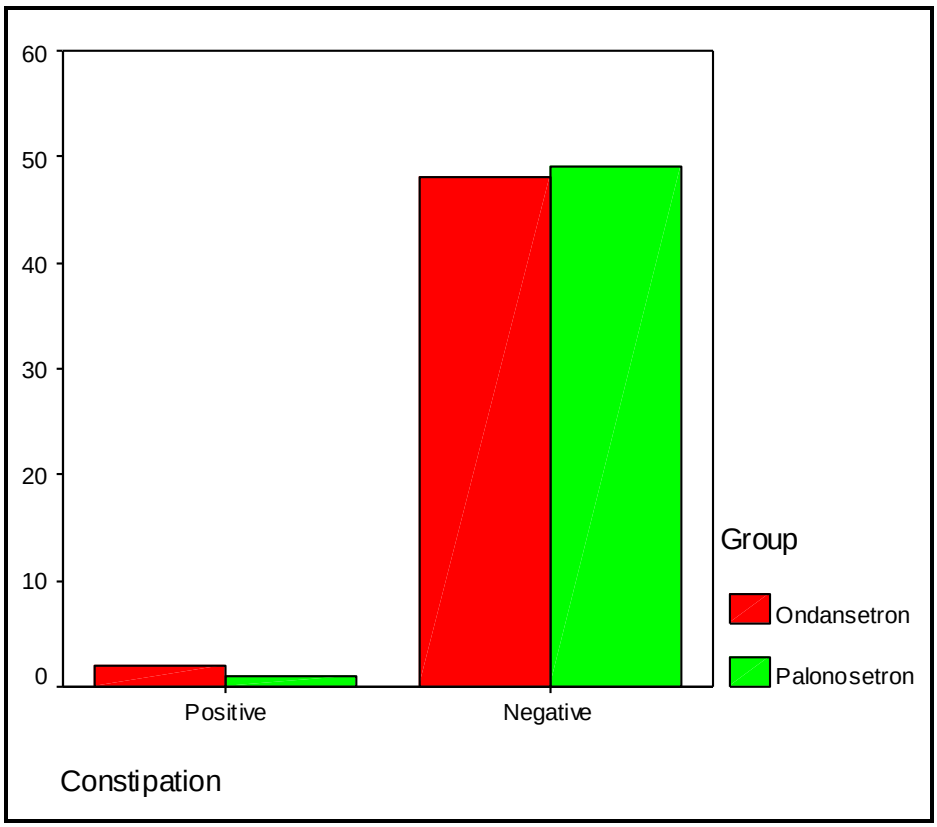


The chart above shows the comparison of the incidence of dizziness between the ondansetron and palonosetron group.

CONSTIPATION

We found that 4% of study subjects in ondansetron group had constipation whereas it was 2% in palonosetron group without any statistical difference(p value 0.558).

CONSTIPATION			
GROUP	**O**	**P**	**P VALUE**
+	2 (4%)	1 (2%)	0.558
-	48 (96%)	49 (98%)	



The chart above shows the comparison of incidence of constipation between the ondansetron and palonosetron group.

DISCUSSION

Nausea and vomiting in the post operative period is a distressing complication following General Anesthesia. Incidence of Nausea and vomiting in the post operative period delays the discharge of the patient undergoing day care surgery.Hence, the search for an effective antiemetic is reflected in the numerous studies that have been carried out so far.

Since the mechanism and the pathway involved in nausea and vomiting is complex, no single drug can serve the purpose of completely preventing nausea and vomiting. The definite risk factors for the incidence of post operative nausea and vomiting include age, gender, duration and the type of anesthesia, obesity, non smokers, meniere's disease , history of motion sickness and history of post operative nausea and vomiting. The increased usage of volatile anesthetics in General anaesthesia and opioids for post operative analgesia have increased the incidence of post operative nausea and vomiting.

Currently 5HT3 receptor antagonists are used as first line antiemetics in the prevention of post operative nausea and vomiting. Among serotonin receptor antagonist, ondansetron is the first drug of choice.

In the present study, the efficacy of Palonosetron is compared with Ondansetron in the prevention of post operative nausea and vomiting in patients undergoing Laparoscopic gynaecological surgery. The risk factor in the subjects include female patients, laparoscopy and gynaecological procedures which is significantly associated with the incidence of nausea and vomiting. In the current era of minimally invasive surgery aiming at discharge on the day of surgery to minimize the cost and improve the quality of life , an effective anti emetic with greater potency and longer half life is required. As discussed above, Palonosetron meets the above criteria and it is superior among the serotonin (5 HT3) receptor antagonist in terms of potency and half life.

In this study, we compared the potency ,antiemetic effect and adverse effect profile of intravenous ondansetron and palonosetron.

.The incidence of vomiting is 34% in the ondansetron group when compared to 10% in the palonosetron group. The incidence of nausea is 16% in Ondansetron group when compared to 4% in the Palonosetron group.

We found that there was no difference in the incidence of nausea and vomiting between the groups in the first 0-2 hours and it is significantly reduced in palonosetron group when compared to ondansetron group in the 2-48 hours.

Bajwas et al reported that post operative vomiting occurred in 13.3% patients in ondansetron group ant it was 3.3% in palonosetron group which is less when compared to our study .The incidence of vomiting in ondansetron and palonosetron group is 20% and 6% in their study when compared to 16% and 4% respectively in our study. Reduction in nausea and emetic episodes in their study could be due to the use of Propofol for induction and maintenance of anaesthesia which posses antiemetic effect even at very low doses. The results of their study correlates with our study which shows that palonosetron is superior to ondansetron in the prevention of nausea and vomiting.

Moon Y et al reported that the incidence of PONV is 62% in ondansetron group compared to 42% in palonosetron group in the study of patients who received opioid based patient controlled analgesia. The incidence of PONV is comparatively higher than in our study .This could be probably due to the continuous use of opioids in the post operative period. The results obtained from the study is similar to our results which proves that palonosetron is superior to ondansetron in the prevention of post operative nausea and vomiting.

We found that the incidence of adverse effect such as headache, constipation and dizziness is similar in both groups This correlates with the reports of other studies in relation to the adverse effect profile of the two drugs under study.

There was no incidence of life threatening rhythm abnormalities like prolonged QT interval in our study. Food and drug administration has recently issued black box alert for ondansetron in view of prolongation of QT interval. However,no such incidence have been reported in palonosetron so far.

Based on observation and analysis, we found that Palonosetron was found to be superior to ondansetron in the prevention of Nausea and vomiting. Second generation drug Palonosetron is unique among the serotonin receptor antagonist because of its allosteric binding at the receptor site with receptor internalization and a prolonged duration of action of around 40 hours.

Hence, single intravenous dose of 0.075mg Palonosetron before induction of anaesthesia is the preferred drug of choice in the prevention of nausea and vomiting

CONCLUSION

It is concluded that Intravenous Palonosetron (75 mcg) is more effective than intravenous Ondansetron(4 mg) in the prevention of post operative nausea and vomiting.The number and frequency of emetic episodes were significantly reduced. Hence palonosetron is superior to ondansetron and it is safe and reliable to use in the prevention of post operative nausea and vomiting.

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PROFORMA

DATE: ROLL NO:

NAME:

AGE: SEX:

IP NO:

DIAGNOSIS:

PLANNED SURGICAL PROCEDURE:

PRE OP ASSESSMENT:

HISTORY: Any Co-morbid illness

H/O Documented Difficult Airway

H/O previous surgeries

Ht: CVS:

Wt: RS:

AIRWAY: MMC - IID -
DENTITION -

INVESTIGATIONS:-

Hb-

RFT-

LFT-

ECG-

CXR-

PRE OP VITALS:

PREMEDICATION DRUGS:

STUDY DRUG:-

INDUCTION:-

INTUBATION:-

MAINTENANCE:-

REVERSAL DRUGS:-

DURATION OF PROCEDURE:-

MEASURES OF STUDY OUTCOME:

INCIDENCE OF PONV: NAUSEA VOMITING RESCUE DRUG.

0-2 HOURS

2-24HOURS

24-48HOURS

DOSE OF OPIODS USED:-

INTRA OP COMPLICATIONS:-

POST OP COMPLICATIONS:-

ADVERSE EFFECT:- HEADACHE/ NAUSEA/ VOMITING.

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

EC Reg No.ECR/270/Inst./TN/2013
Telephone No : 044 25305301
Fax: 044 25363970

CERTIFICATE OF APPROVAL

To

Dr.L.Pavithra,
Postgraduate in Anaesthesiology,
Institute of Anaesthesiology and Critical Care,
Rajiv Gandhi Govt. General Hospital
Madras Medical College, Chennai-3.

Dear **Dr. L.Pavithra,**

The Institutional Ethics Committee of Madras Medical College, reviewed and discussed your application for approval of the proposal entitled **"Comparative Evaluation of intravenous ondansetron (4mg) Versus intravenous palonosetron (75mcg) in the prevention of postoperative nausea and vomiting in laparoscopic gynaecological surgeries"** No.01042014.

The following members of Ethics Committee were present in the meeting held on 08.04.2014 conducted at Madras Medical College, Chennai-3.

1.	Dr. C.Rajendran, M.D,	-- Chairperson
2.	Prof. Kalaiselvi, M.D, Vice Principal, MMC, Ch-3	-- Member Secretary
3.	Prof. Nandhini, M.D, Inst. of Pharmacology, MMC, Ch-3	-- Member
4.	Prof.Bhavani Sankar, M.S, Prof & HOD General Surgery, MMC, Ch-3	-- Member
5.	Prof.V.Padmavathi, M.D, I/c. Director of Pathology, MMC, Ch-3	-- Member
6.	Thiru. S. Govindasamy, BA., BL	-- Lawyer
7.	Tmt.Arnold Saulina, MA MSW	-- Social Scientist
8.	Thiru.S.Ramesh Kumar, Administrative Officer, MMC, Ch-3.	-- Lay Person

We approve the proposal to be conducted in its presented form.

Sd/Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

23/4/14

CHENNAI-600 003

INFORMATION TO PARTICIPANTS

Investigator **:** Dr.L.PAVITHRA.

Name of the Participant:

Title :

"**Comparative Evaluation of Intravenous Ondansetron(4mg) Versus Intravenous Palonosetron (75mcg) in the Prevention of Postoperative Nausea and Vomiting in Laparoscopic Gynaecological Surgeries "**

You are invited to take part in this research study. We have got approval from the IEC. Your are asked to participate because you satisfy the eligibility criteria .We want to compare and study the efficacy of intravenous ondansetron Versus intravenous palonosetron in the prevention of post operative nausea and vomiting.

What is the Purpose of the Research:

For laparoscopic gynaecological surgeries, antiemetic drug, either ondansetron or palonosetron will be given just before the induction of anaesthesia. The study is done to compare the efficacy of ondansetron and palonosetron with respect to

1. Incidence of post operative nausea and vomiting.
2. Post operative requirement of rescue anti emetic.

The Study Design:

All the patients in the study will be divided into two groups.

Group O - pre operative intravenous ondansetron.

Group P- pre operative intravenous palonosetron.

All patients will be given general anaesthesia.

Benefits

Ondansetron and palonosetron given pre operatively before the induction of anesthesia reduces the incidence of post operative nausea and vomiting.

Discomforts and risks

Discomfort during injection such as pain,redness and burning may be present.

Other rare adverse events include headache, light headedness, transient elevation of liver enzymes and very rarely rythm disturbance.

This intervention has been shown to be well tolerated as shown by previous studies. And if you do not want to participate you will have alternative standard treatment and your safety is our prime concern.

Time :
Date :
Place :

Signature / Thumb Impression of Patient
Patient Name:

Signature of the Investigator : _____

Name of the Investigator : _____

PATIENT CONSENT FORM

Study Title: "**Comparative Evaluation of Intravenous Ondansetron (4mg) Versus Intravenous Palonosetron (75mcg) in the Prevention of Postoperative Nausea and Vomiting in Laparoscopic Gynaecological Surgeries "**

Study center: Institute of Anaesthesiology and Critical Care,
Govt Kasturba Gandhi Hospital for Women and Children,
Madras Medical College, Chennai 600003.

Participant Name : Age: Sex: I.P.No:

I confirm that I have understood the purpose and procedure of the above mentioned study.I have the opportunity to ask the question and all my questions and doubts have been answered to my satisfaction.

I have been explained about the safety, advantage and disadvantage of the drugs used.

I understand that my participation in the study is voluntary and that I am free to withdraw at anytime without giving any reason.

I understand that the investigator, regulatory authorities and the ethical committee will not need my permission to look at my health records both in respect to current study and any further research that may be conducted in relation to it, even if I withdraw from the study . I understand that my identity will not be revealed in any information released to third parties or published journal , unless as required under the law . I agree not to restrict the use of any data or results that arise from the study .

Time:
Date: Signature / thumb impression of patient

Place: Patient name:

Signature of the investigator:

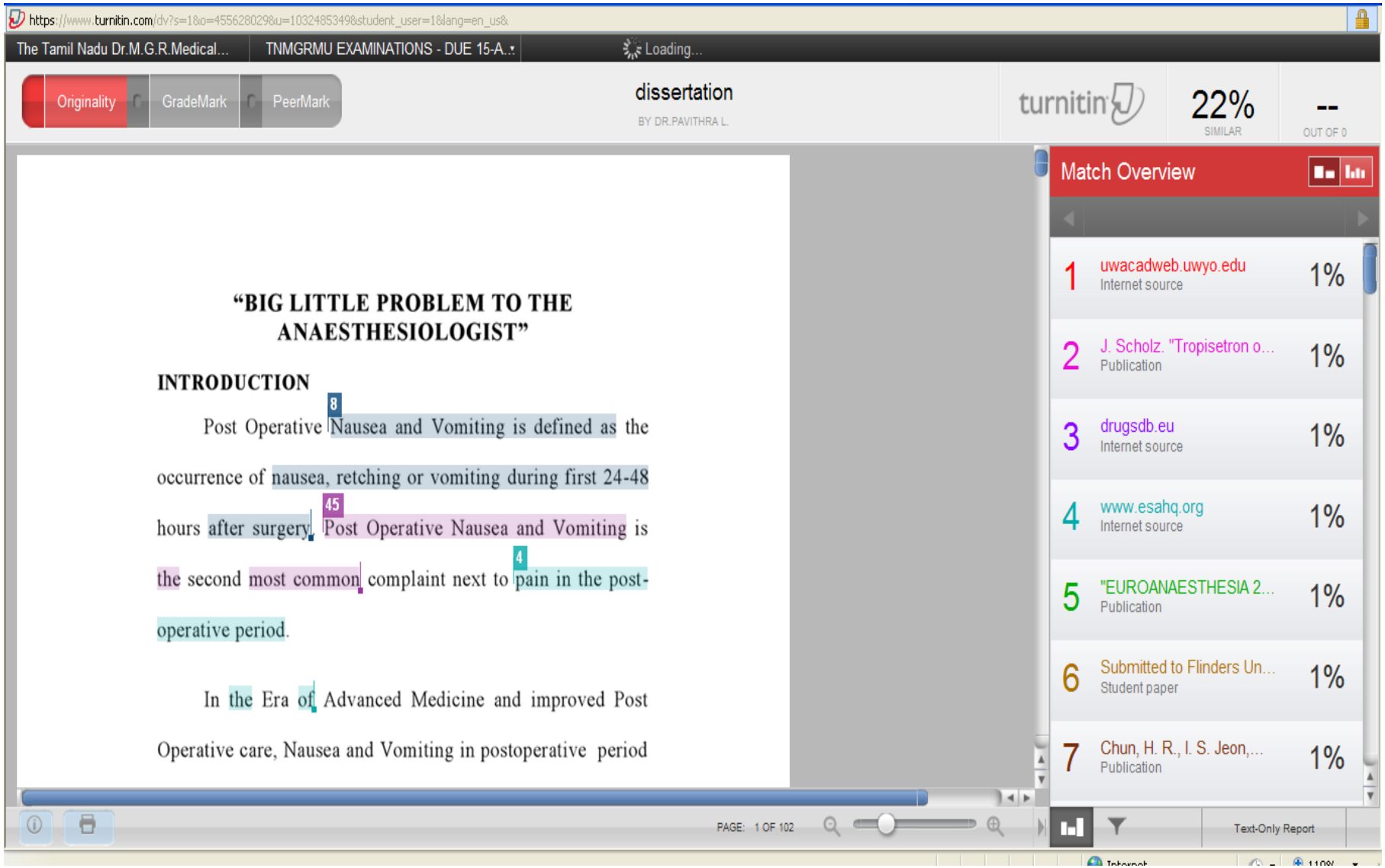
Name of the investigator:

S.no	Name	Age	Weight	Diagnosis	Surgery	Duration sx	uration an	0/P	ASA	0-2/v	2-24/v	24-48/v	0-2/n	2-24/n	24-48/n	headache	dizziness	constipation
1	Malar	24	48 kg	PCOD	DLAP	35 mins	50 mins	O	1									
2	kannagi	54	49	OVARIAN MA	DLAP	43	64	O	2	+				+				
3	seetha	36	45	ENDOMETRIC	DLAP	55	73	O	1							+		
4	murugavalli	35	66	PCOD	LAP DRILLING	46	74	O	1				+					
5	rani	58	47	AUB	LAVH	122	134	O	2								+	
6	ramila	28	56	INFERTILITY	DHL	38	52	O	1	+		+						
7	thangam	28	59	FP	LS	42	58	O	1									
8	poonkodi	38	64	AUB	DHL	55	63	O	1	+								+
9	yazhisai	37	65	AUB	DHL	57	71	O	1						+			
10	azhagu	21	35	FP	LS	44	58	O	1									
11	ranjana	25	53	INFERTILITY	DHL	53	62	O	1									
12	reena	48	64	AUB	DHL	58	69	O	2	+			+					
13	nila	52	66	DUB	LAVH	102	122	O	2									
14	radha	55	56	OVARIAN MA	DLAP	64	81	O	2							+		
15	ranjitha	26	55	PCOD	LAP DRILLING	83	102	O	1		+							
16	renuka	33	60	INFERTILITY	DHL	42	58	O	1	+				+				
17	yamini	27	47	ENDOMETRIC	DHL	47	67	O	1									
18	pallavi	47	48	AUB	DLAP	53	62	O	2								+	
19	santhya	25	53	INFERTILITY	DHL	43	56	O	1			+						
20	seetha	27	52	FP	LS	38	43	O	1									
21	sanjana	44	55	OVARIAN MA	DLAP	87	102	O	1	+			+					
22	devi	48	58	DUB	LAVH	123	132	O	1		+							
23	azhamelu	25	59	FP	LS	38	54	O	1									+
24	annakili	59	66	OVARIAN MA	DLAP	121	144	O	2									
25	maadhavi	43	65	FIBROID UTE	LAP MYOMEC	94	108	O	1							+		
26	manjula	44	69	AUB	DHL	43	63	O	1									
27	panjaangam	28	72	INFERTILITY	DHL	52	72	O	1									
28	valarmathi	27	74	FP	LS	33	48	O	1									
29	archana	19	54	PCOD	LAP DRILLING	81	103	O	1		+							
30	annakili	35	62	INFERTILITY	DHL	42	64	O	1									
31	banu	33	67	FP	LS	53	66	O	1									
32	kumari	34	55	AUB	DHL	64	83	O	1	+								
33	kanjana	38	54	ENDOMETRIC	LAP DRILLING	121	132	O	1					+	+			
34	rekha	47	53	DUB	LAVH	154	168	O	2									
35	ambujam	44	58	AUB	DHL	43	66	O	2									

S.no	Name	Age	Weight	Diagnosis	Surgery	Duration sx	uration an	0/P	ASA	0-2/v	2-24/v	24-48/v	0-2/n	2-24/n	24-48/n	headache	dizziness	constipation
36	selvi	26	54	FP	LS	52	67	O	1		+						+	
37	shanthi	55	64	DUB	LAVH	121	143	O	2			+						
38	ragavi	58	67	OVARIAN MA	DLAP	93	107	O	2									
39	meena	25	59	FP	LS	62	74	O	1									
40	uma	27	43	INFERTILITY	DHL	51	77	O	1									
41	maragatham	28	48	FIBROID UTE	LAP MYOMEC	58	73	O	1									
42	muniyammal	38	46	AUB	DHL	62	82	O	1									
43	solai	20	54	FP	LS	43	66	O	1				+					
44	valli	46	58	DUB	LAVH	121	150	O	1									
45	vanaja	47	52	DUB	LAVH	104	125	O	1	+						+		
46	lakshmi	28	34	FP	LS	33	53	O	1									
47	vijaya	55	38	OVARIAN MA	LAVH	114	133	O	2		+							
48	packiya	52	36	DUB	LAVH	102	132	O	2									
49	pangajam	22	38	PCOD	LAP DRILLING	88	108	O	1	+								
50	raani	35	58	FIBROID UTE	MYOMECTON	120	132	P	1		+							

S.no	Name	Age	Weight	Diagnosis	Surgery	Duration sx	Duration anes	0/P	ASA	0-2/v	2-24/v	24-48/v	0-2/n	2-24/n	24-48/n	headache	dizziness	constipation
1	subha	23	42	FP	LS	38	54	P	1									
2	thiruselvi	46	48	AUB	DHL	44	63	P	1	+								
3	muthukumari	45	51	AUB	DHL	36	56	P	1				+					
4	saveetha	23	47	INFERTILITY	DHL	53	67	P	1									
5	meena	26	48	FP	LS	27	48	P	1									
6	maragatham	22	55	ENDOMETRIOSIS	LAP DRILLING	62	82	P	1									
7	revathi	35	59	FIBROID UTERUS	LAP MYOMECTOMY	53	86	P	1									
8	raaji	34	54	AUB	DHL	44	64	P	1									
9	muthulakshmi	32	38	FP	LS	28	43	P	1									
10	viji	32	46	INFERTILITY	DHL	54	72	P	1									
11	saroja	44	49	AUB	DHL	53	71	P	2	+						+		
12	poomayil	48	54	DUB	LAVH	101	143	P	2									
13	vasantha	54	55	INFERTILITY	DHL	46	64	P	2									+
14	kutty	27	58	FP	LS	33	46	P	1									
15	vaani	33	49	AUB	DHL	54	72	P	2									
16	pooja	34	58	DUB	LAVH	92	133	P	1									
17	poongaothai	42	64	AUB	DHL	44	57	P	2									
18	mariammal	45	67	DUB	LAVH	113	126	P	1									
19	rameswari	25	49	FP	LS	27	47	P	1								+	
20	nandhini	28	53	FP	LS	24	32	P	1									
21	jeya	35	47	FIBROID UTERUS	LAVH	77	110	P	1									
22	janaki	37	58	AUB	DHL	38	51	P	1									
23	amala	44	69	AUB	DHL	46	53	P	1		+							
24	ambiga	48	72	DUB	LAVH	93	132	P	2									
25	sujatha	54	64	OVARIAN MASS	DLAP	83	104	P	2									
26	selvi	53	66	OVARIAN MASS	DLAP	86	107	P	2	+								
27	saadhana	45	68	AUB	DHL	53	77	P	1									
28	ramila	24	59	FP	LS	32	48	P	1									
29	aandal	26	64	FP	LS	28	43	P	1				+			+		
30	anjana	23	67	INFERTILITY	DHL	46	64	P	1									
31	bavya	28	62	FIBROID UTERUS	LAP MYOMECTOMY	92	113	P	1									
32	tamilselvi	35	66	INFERTILITY	DHL	46	62	P	1									
33	malathi	36	67	DUB	LAVH	121	141	P	1									
34	moogambikai	44	53	AUB	DHL	113	126	P	2									
35	mallika	45	55	DUB	LAVH	102	124	P	2									
36	jeyashree	48	58	AUB	DHL	33	48	P	2									

S.no	Name	Age	Weight	Diagnosis	Surgery	Duration sx	Duration anes	0/P	ASA	0-2/v	2-24/v	24-48/v	0-2/n	2-24/n	24-48/n	headache	dizziness	constipation
37	raani	52	52	DUB	LAVH	110	126	P	2								+	
38	amirthavalli	34	49	INFERTILITY	DHL	36	47	P	1									
39	anandhalakshmi	37	47	DUB	LAVH	121	134	P	1									
40	shobana	36	69	AUB	DHL	44	56	P	1									
41	rajaathi	25	63	INFERTILITY	DHL	38	48	P	1									
42	meyyamai	45	56	AUB	DHL	44	64	P	2									
43	manjula	23	59	FP	LS	33	48	P	1									
44	malarvizhi	28	51	PCOD	LAP DRILLING	81	114	P	1									
45	arasi	35	54	AUB	DHL	44	63	P	1	+						+		
46	prabhavathi	43	62	DUB	LAVH	98	108	P	1								+	
47	jeyanthi	28	71	FP	LS	42	56	P	1									
48	nirmala	34	74	ENDOMETRIOSIS	DLAP	61	77	P	1									
49	niranjana	29	72	FIBROID UTERUS	LAP MYOMECTOMY	76	93	P	1									
50	mythrayee	25	70	FP	LS	25	45	P	1									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"BIG LITTLE PROBLEM TO THE ANAESTHESIOLOGIST"
INTRODUCTION
Post Operative Nausea and Vomiting is defined as the occurrence of nausea, retching or vomiting during first 24-48 hours after surgery. Post Operative Nausea and Vomiting is the second most common complaint next to pain in the post-operative period.
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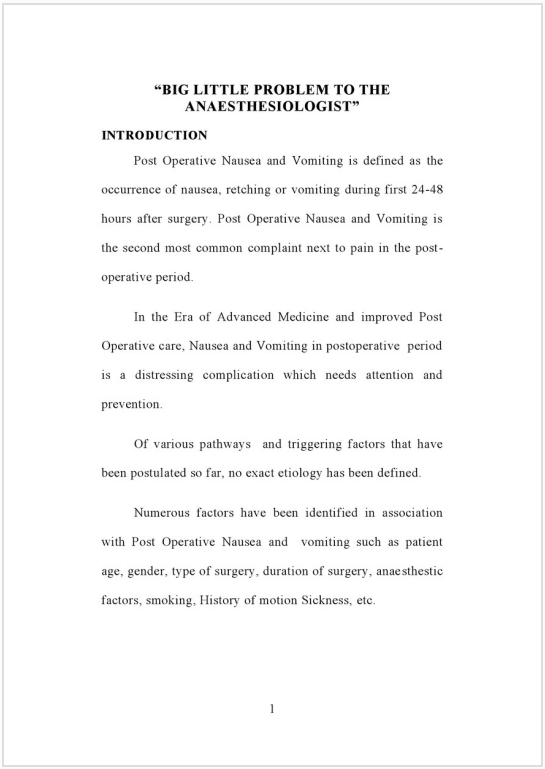

"BIG LITTLE PROBLEM TO THE ANAESTHESIOLOGIST"

INTRODUCTION

Post Operative Nausea and Vomiting is defined as the occurrence of nausea, retching or vomiting during first 24-48 hours after surgery. Post Operative Nausea and Vomiting is the second most common complaint next to pain in the post-operative period.

In the Era of Advanced Medicine and improved Post Operative care, Nausea and Vomiting in postoperative period is a distressing complication which needs attention and prevention.

Of various pathways and triggering factors that have been postulated so far, no exact etiology has been defined.

Numerous factors have been identified in association with Post Operative Nausea and vomiting such as patient age, gender, type of surgery, duration of surgery, anaesthestic factors, smoking, History of motion Sickness, etc.

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